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Moyer, Elizabeth
Hirtzer, Pamela

Point of Contact:
Beverly Sheers
Technical Info. Specialist
CM1 12C14 Tel: 308-4994

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PTO-1590 (9-90)

Devi, S
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09/393590

- key terms

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                 "PHOSPHATE (32PO4)"/CN OR "PHOSPHATE (H2PO4-)"/CN OR
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                 ("PHOSPHATE (P5O143-)"/CN OR "PHOSPHATE (P6O186-)"/CN)
L2             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  CITRATE/CN
L3             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  SUCCINATE/CN
L4            10 SEA FILE=REGISTRY ABB=ON  PLU=ON  L1 OR L2 OR L3


L5             2 SEA FILE=REGISTRY ABB=ON  PLU=ON  "BOTULINUM TOXIN D"/CN
                 OR "BOTULINUM TYPE E TOXIN (CLOSTRIDIUM BUTYRICUM STRAIN
                 BL6340 LIGHT CHAIN REDUCED)"/CN


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L3             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  SUCCINATE/CN
L4            10 SEA FILE=REGISTRY ABB=ON  PLU=ON  L1 OR L2 OR L3
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                 BT(S)BOTULINUM OR L5
L7            39 SEA FILE=CAPLUS ABB=ON  PLU=ON  L6 AND BUFFER?
L8            18 SEA FILE=CAPLUS ABB=ON  PLU=ON  L7 AND (L4 OR PHOSPHATE
                 OR CITRATE OR SUCCINATE)


L5             2 SEA FILE=REGISTRY ABB=ON  PLU=ON  "BOTULINUM TOXIN D"/CN
                 OR "BOTULINUM TYPE E TOXIN (CLOSTRIDIUM BUTYRICUM STRAIN
                 BL6340 LIGHT CHAIN REDUCED)"/CN
L6          1248 SEA FILE=CAPLUS ABB=ON  PLU=ON  BOTULINUM TOXIN OR
                 BT(S)BOTULINUM OR L5
L11          113 SEA FILE=CAPLUS ABB=ON  PLU=ON  L6 AND (FORMUL? OR
                 COMPOSITION OR COMP##)
L12            4 SEA FILE=CAPLUS ABB=ON  PLU=ON  L11 AND BUFFER?


L13           20 L8 OR L12

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L13 ANSWER 1 OF 20 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:190943 CAPLUS
DOCUMENT NUMBER: 132:227422
TITLE: Stable liquid **formulations** of **Botulinum toxin**
INVENTOR(S): Moyer, Elizabeth; Hirtzer, Pamela
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000015245	A2	20000323	WO 1999-US20912	19990909
WO 2000015245	A3	20000608		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9958214	A1	20000403	AU 1999-58214	19990909
PRIORITY APPLN. INFO.:			US 1998-99870	19980911
			WO 1999-US20912	19990909

AB The invention includes liq. **formulations** of **botulinum toxin** that are stable to storage in liq. form at std. refrigerator temps. for at least 1-2 yr and to storage at higher temps. for at least 6 mo. The invention also includes methods of treatment using such **formulations** and uses of such **formulations** in the manuf. of medicaments for various therapeutic and cosmetic treatments. A **formulation** was prepd. contg. **Botulinum toxin** Type B 500.+-.100 LD50U/mL, di-Na **succinate** 10 mM, NaCl 100 mM, human albumin 0.5 mg/mL, and HCl for pH adjustment.

IT **126-44-3**, **Citrate**, biological studies
14265-44-2, **Phosphate**, biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stable liq. **formulations** of **Botulinum toxin**)

L13 ANSWER 2 OF 20 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:425354 CAPLUS
DOCUMENT NUMBER: 131:224672
TITLE: Detection of sparse **botulinum**

toxin A binding sites using fluorescent latex microspheres

AUTHOR(S): Crosland, Richard D.; Canziani, Gabriela A.
CORPORATE SOURCE: Toxinology Division, United States Army Medical Research Institute of Infectious Diseases, Frederick, MD, 21702, USA

SOURCE: J. Histotechnol. (1999), 22(2), 113-115
CODEN: JOHIDN; ISSN: 0147-8885
PUBLISHER: National Society for Histotechnology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The most potent toxins known are produced by strains of Clostridium botulinum. To paralyze the vertebrate neuromuscular junction, the toxins bind selectively to nerve endings, translocate into the presynaptic terminal, and hydrolyze proteins of the exocytotic app., thus inhibiting the release of acetylcholine. Our goal was to develop a convenient, reliable technique to detect specific binding of **botulinum toxin** A to its targets, a technique that could be easily modified to detect the binding sites of other ligands as well. Our method utilized fluorescent latex microspheres and is theor. capable of detecting a single binding site at the light microscopic level. Nonspecific binding sites on 7-.mu.m thick sections of unfixed, cryosectioned mouse diaphragm were first blocked with 20% goat serum in **phosphate-buffered** saline (GS/PBS). We incubated the diaphragm for 1 h at 22.degree. with various concns. of **botulinum toxin** A in GS/PBS, followed by incubation with rabbit anti-**botulinum toxin** A antiserum, biotin-labeled goat anti-rabbit antibody, and finally avidin-labeled, 0.03 .mu.m diam., fluorescent latex microspheres. As expected, binding was localized to the area of the neuromuscular junction. Binding was also obsd. in assocn. with axons innervating some junctions. We could detect binding on diaphragms that were exposed to as little as 10 pM **botulinum toxin** A, which is in the low range of effective in vitro doses that block neuromuscular transmission. This is a convenient, sensitive, and specific technique for detecting **botulinum toxin** A binding sites that is easily modifiable for the detection of binding sites of other ligands as well.

REFERENCE COUNT: 12
REFERENCE(S):
(1) Black, J; J Cell Biol 1986, V103, P521 CAPLUS
(2) Black, J; J Cell Biol 1986, V103, P535 CAPLUS
(4) Dolly, J; Nature 1984, V307, P457 CAPLUS
(5) Dolly, J; Toxicon 1982, V20, P141 CAPLUS
(6) Hanig, J; J Theor Biol 1979, V77, P107 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 20 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1994:242760 CAPLUS
DOCUMENT NUMBER: 120:242760
TITLE: An ELISA for detection of botulinal toxin types A, B, and E in inoculated food samples
AUTHOR(S): Potter, Marianne D.; Meng, Jianghong; Kimsey, Paul
CORPORATE SOURCE: Westreco/Nestle, New Milford, CT, 06776, USA
SOURCE: J. Food Prot. (1993), 56(10), 856-61
CODEN: JFPRDR; ISSN: 0362-028X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An ELISA was developed to screen for the presence of botulinal toxin types A, B, and E in inoculated food studies. A com. available trivalent antitoxin (Connaught Labs., Ontario) was used as a capture antibody and biotinylated for use as a secondary antibody. An avidin-alk. phosphatase conjugate coupled with an enzyme-based amplification system resulted in a high degree of sensitivity. Detection levels of purified neurotoxins in gelatin **phosphate buffer** were 9 LD50 for type A and <1 i.p. mouse LD50 for types B and E, resp. Toxin produced by two-type F strains (proteolytic and nonproteolytic) was detected in a liq. lab. medium. In a comparative study of over 490 samples of ground turkey meat inoculated with C. botulinum types E and nonproteolytic B, the ELISA gave no false negatives and 91 false positives. False positives were thought to be due to the presence of inactivated toxin or toxin levels insufficient to cause mouse death. Statistical anal. of these data showed an ELISA sensitivity of 100%, specificity of 70.6%, and an efficiency of 81.4% when compared to the mouse bioassay for detection of botulinal toxins types B and E. Coffee intermediates inoculated with proteolytic Clostridium botulinum types A and B caused nonspecific death in mice but were neg. for presence of toxin by ELISA.

L13 ANSWER 4 OF 20 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1986:474118 CAPLUS
DOCUMENT NUMBER: 105:74118
TITLE: Binding of Clostridium botulinum neurotoxin to gangliosides
AUTHOR(S): Ochanda, James O.; Syuto, Bunei; Ohishi, Iwao; Naiki, Masaharu; Kubo, Shuichiro
CORPORATE SOURCE: Fac. Vet. Med., Hokkaido Univ., Sapporo, 060, Japan
SOURCE: J. Biochem. (Tokyo) (1986), 100(1), 27-33
CODEN: JOBIAO; ISSN: 0021-924X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The binding characteristics of C. botulinum neurotoxins of types B, C1, and F of gangliosides was studied by TLC plate and microtiter

plate methods at low (10 mM NaCl in 10 mM Tris-HCl **buffer**, pH 7.2) or high (150 mM NaCl in 1/ mM Tris-HCl **buffer**, pH 7.2) ionic strengths and at 0 or 37.degree.. The 3 types of toxins bound exclusively to 3 kinds of gangliosides, GD1a [12707-58-3], GD1b [19553-76-5] and GT1b [59247-13-1], in both the TLC plate and the microtiter plate methods. Type C1 toxin bound to the 3 gangliosides under all the conditions, while type B and F toxins bound only at low ionic strength and 37.degree.. At low ionic strength, the binding kinetics for the 3 toxins was monophasic in Scatchard plots, and the assocn. consts. obtained in the microtiter plate system were 2-4 .times. 108/M. In contrast, the binding kinetics of type C1 toxin in high ionic strength was biphasic in the Scatchard plot, and 2 assocn. consts. were obtained in the microtiter plate system. The heavy chain facilitated the binding of the toxin to the gangliosides. Thus, different types of **botulinum toxins** bind to the gangliosides under different optimal conditions and the gangliosides may not be the common receptor for all types of bobulin toxins. The gangliosides may bind to type C1 toxin together with other potential receptor(s) on synaptosomal membranes.

L13 ANSWER 5 OF 20 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1982:117223 CAPLUS
DOCUMENT NUMBER: 96:117223
TITLE: Purification and oral toxicities of Clostridium botulinum progenitor toxins
AUTHOR(S): Sakaguchi, Genji; Ohishi, Iwao; Kozaki, Shunji
CORPORATE SOURCE: Coll. Agric., Univ. Osaka Prefect., Sakai, 591, Japan
SOURCE: Biomed. Aspects Botulism, [Proc. Int. Conf.] (1981), 21-34. Editor(s): Lewis, George E., Jr. Academic: New York, N. Y.
CODEN: 47GRAE
DOCUMENT TYPE: Conference
LANGUAGE: English

AB The article describes methods for purifn. of the title group I-III progenitor toxins, their mol. structure, oral toxicities, and the intestinal absorption of the botulin toxin in relation to mol. structure. Cation exchangers such as CO-carboxymethyl- and sulfopropyl-Sephadex were used to purify the progenitor toxins. Type A progenitor toxin involves 3 different mol. forms 19S, 16S, and 12S, type B, C, and D 2 forms 16S and 12S, and type E a single form 12S or 10S. All the progenitor toxins, when subjected to DEAE-Sephadex chromatog. or sucrose-d. gradient ultracentrifugation at pH 7.5-8 were sepd. into toxic and nontoxic components. The toxic component was uniform in the mol. size, being 7S (5.6S for type F), regardless of the mol. size of the parenteral progenitor toxin. The mol. dissocn. of the progenitor toxin was reversible. When the toxic and nontoxic components at equimolar ratio were mixed

and the mixt. is dialyzed against 0.05M **phosphate buffer** (pH 6), mol. reassocn. occurs forming mols. indistinguishable from the parental progenitor toxin. Absorption studies showed that the progenitor toxin does not dissoc. in the duodenum; the whole mol. is absorbed through the intestinal wall without dissocn.

L13 ANSWER 6 OF 20 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1981:190537 CAPLUS
DOCUMENT NUMBER: 94:190537
TITLE: Thermal inactivation of Clostridium **botulinum toxin** types F and G in **buffer** and in beef and mushroom patties
AUTHOR(S): Bradshaw, J. G.; Peeler, J. T.; Twedt, R. M.
CORPORATE SOURCE: Div. Microbiol., Food Drug Adm., Cincinnati, OH, 45226, USA
SOURCE: J. Food Sci. (1981), 46(3), 688-90, 696
CODEN: JFDSAZ; ISSN: 0022-1147
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The time-temp. relations for the inactivation of crude toxins prepd. from C. botulinum type F strain Wall 8 and type G strain G89 were detd. in three different heating menstrua. Toxins dild. to 7700-32,000 mouse LD50 units/0.5 mL in beef and mushroom patties (pH 6.05), 0.1M **phosphate buffer** (pH 6.05), or 0.1M acetate **buffer** (pH 5.0) were heated at 65.6-76.7.degree.. In the beef patties, inactivation times were 108.1-1.6 min (values from low to high temp. treatment) for type F toxin, and 158.8-1.8 min for type G toxin. Less time was required in **phosphate buffer**.

L13 ANSWER 7 OF 20 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1981:187268 CAPLUS
DOCUMENT NUMBER: 94:187268
TITLE: Separation and characterization of heavy and light chains from Clostridium botulinum type C toxin and their reconstitution
AUTHOR(S): Syuto, Bunei; Kubo, Shuichiro
CORPORATE SOURCE: Fac. Vet. Med., Hokkaido Univ., Sapporo, 060, Japan
SOURCE: J. Biol. Chem. (1981), 256(8), 3712-17
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB C. botulinum Type C toxin consists of a heavy and a light chain with mol. wts. of 98,000 and 53,000, resp., which are linked by 1 disulfide bond. The 2 components were sepd. from each other by QAE-Sephadex A-50 column chromatog. by stepwise elution with NaCl in

27.5 mM borax-45 mM NaH2PO4 **buffer**, pH 8.0, contg. 5% 2-mercaptoethanol at 0.degree.. The purified components had different amino acid **compns**. and antigenicities, and the toxicity of the toxin was neutralized completely by either anti-heavy chain Fab or anti-light chain Fab. The 2 components could be reconstituted to form an active mol. with recovered toxicity which varied according to the method used. Max. recovery was obtained in a system in which the intersubunit disulfide bond was 1st formed in the presence of a high concn. of neutral salts, after which the salt concn. was gradually decreased. The reconstituted prepn. was highly toxic and had the same properties as the parental toxin on chromatog., SDS-polyacrylamide gel electrophoresis, and immunodiffusion. By the use of 3 perturbants, the fractions of exposed tryptophans and tyrosines of the prepn. were found to be almost the same as that of the parental toxin.

L13 ANSWER 8 OF 20 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1981:42392 CAPLUS
DOCUMENT NUMBER: 94:42392
TITLE: Isolation and properties of highly purified type F Clostridium **botulinum toxin**
AUTHOR(S): Uvarova, R. N.; Reshetnikova, L. N.; Ispolatovskaya, M. V.; Bulatova, T. I.
CORPORATE SOURCE: Inst. Epidemiol. Mikrobiol., Moscow, USSR
SOURCE: Zh. Mikrobiol., Epidemiol. Immunobiol. (1980), (11), 42-6
CODEN: ZMEIAV; ISSN: 0372-9311
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB The steps involved in the isolation of C. **botulinum toxin** were initial pptn. with (NH4)2SO4 or Na hexametaphosphate after cultivation of the culture for 4 days at 28.degree., ultrafiltration through amicon membrane, gel filtration on 2 sephadex G-100 columns and elution with pH 5.6 Na **phosphate-phosphate buffer**, chromatog. on DEAE-cellulose, dialysis in a pH 4.2 acetate **buffer** contg. 0.1 M NaCl, chromatog. on SP-sephadex (C-50), repeating of dialysis, ultrafiltration and then gel filtration on sephadex G-200, and finally dialysis and chromatog. on DEAE-cellulose. The activity of the purified toxin ranged 1.5-4 .times. 107 (min. LD)/mg protein and had a mol. wt. of 50,000 daltons.

L13 ANSWER 9 OF 20 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1980:39964 CAPLUS
DOCUMENT NUMBER: 92:39964
TITLE: Thermal inactivation of Clostridium **botulinum toxins** types A and B in **buffer**, and beef and mushroom patties

AUTHOR(S): Bradshaw, J. G.; Peeler, J. T.; Twedt, R. M.
CORPORATE SOURCE: Div. Microbiol., Food Drug Adm., Cincinnati, OH, 45226, USA
SOURCE: J. Food Sci. (1979), 44(6), 1653-7
CODEN: JFDSAZ; ISSN: 0022-1147
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To det. the time-temp. relations for the inactivation of **botulinum toxins**, crude toxins were prepd. from 3 type A strains (62A, 73A, V141) and 2 type B strains (Beans-B and 999B). Toxins were dild. to 6700-32,000 mouse LD50 units/0.5 mL in beef and mushroom patties, and in 0.1M **phosphate buffer**, both at pH 6.05, and 0.1M acetate **buffer**, pH 5.0, and were heated at 67.8-80.0.degree.. In the patties, inactivation times were 53.15-0.62 min and 51.20-1.08 min for the most thermostable type A (73A) and type B (Beans-B) toxins, resp., whereas significantly less time was required in **phosphate buffer**.

L13 ANSWER 10 OF 20 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1979:518322 CAPLUS
DOCUMENT NUMBER: 91:118322
TITLE: Structure and toxicity of Clostridium botulinum type C Toxin
AUTHOR(S): Syuto, Bunei; Kubo, Shuichiro
CORPORATE SOURCE: Fac. Vet. Med., Hokkaido Univ., Sapporo, 060, Japan
SOURCE: Jpn. J. Med. Sci. Biol. (1979), 32(2), 132-3
CODEN: JJMCAQ; ISSN: 0021-5112
DOCUMENT TYPE: Journal
LANGUAGE: English

AB C. **botulinum Toxin** C could be sepd. into 2 peptide chains by chromatog. of QAE-Sephadex A-50 with a linear gradient of NaCl in 6% 2-mercaptoethanol-borate **phosphate buffer** at pH 8.1 and 0.degree.. The components had different antigenicities and antitoxin to either chain neutralized the mother toxin toxicity. Combining the 2 chains gave an active form having 74% of the toxicity of the mother toxin; thus both chains are essential for toxicity. The reconstitution method affected the toxicity of the material prepd. from the chains. Tryptophan and tyrosine residues were crit. to maintain the toxin toxicity.

L13 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1979:401071 CAPLUS
DOCUMENT NUMBER: 91:1071
TITLE: Studies on the stability of purified and crude **botulinum toxin** of serotype B (strain ATCC 7949)

AUTHOR(S): Schwarz, W.
CORPORATE SOURCE: Inst. Lebensmittelkd., Fleischhyg. und -Technol., Tieraerztl. Hochsch. Hannover, Hannover, Fed. Rep. Ger.
SOURCE: Arch. Lebensmittelhyg. (1979), 30(1), 29-33
CODEN: ALMHAO; ISSN: 0003-925X
DOCUMENT TYPE: Journal
LANGUAGE: German
AB Crude and purified Clostridium **botulinum toxin** serotype B was stable for 2 wk in pH 4.5 0.05-0.1M **phosphate buffer**. Within the next 2 wk the toxicity decreased only slightly.

L13 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1978:506193 CAPLUS
DOCUMENT NUMBER: 89:106193
TITLE: Heat inactivation of **botulinum toxin** type A in some convenience foods after frozen storage
AUTHOR(S): Woolford, A. L.; Schantz, E. J.; Woodburn, M. J.
CORPORATE SOURCE: Food Res. Inst., Univ. Wisconsin, Madison, Wis., USA
SOURCE: J. Food Sci. (1978), 43(2), 622-4
CODEN: JFDSAZ; ISSN: 0022-1147
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cryst. type A toxin from the Hall Strain of Clostridium botulinum was added to beef pie fillings (pH 5.9), 0.05 M **phosphate buffer** (pH 5.9), cream of mushroom soup (pH 6.2) or tomato soup (pH 4.1), and 1 mL of each sample was placed in 2-mL thin glass ampules. These were frozen and stored at -20.degree. for 180 days. The potency of the toxin remained the same throughout the frozen storage. Although the literature reports show a decrease in the heat stability of type E toxin after frozen storage, the heat inactivation rates for type A remained the same. PH affected the heat stability of type A toxin dissolved in various **buffers**, being greater at lower pH values.

L13 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1976:400877 CAPLUS
DOCUMENT NUMBER: 85:877
TITLE: Extraction and concentration of Clostridium **botulinum toxins** from specimens
AUTHOR(S): Sonnenschein, B.; Bisping, W.
CORPORATE SOURCE: Inst. Mikrobiol. Tierseuchen, Tieraerztl. Hochsch. Hannover, Hannover, Ger.
SOURCE: Zentralbl. Bakteriol., Parasitenkd., Infektionskr. Hyg., Abt. 1: Orig., Reihe A

(1976), 234(2), 247-59
CODEN: ZMMPAO
DOCUMENT TYPE: Journal
LANGUAGE: German
AB C. **botulinum toxins** A-E were added to canned green beans dild. 1:2 with 0.1M **phosphate buffer**, pH 6. The prepn. was homogenized and centrifuged at 4000 rpm for 30 min. Fifteen ml of the supernatant was concd. by Millipose ultrafiltration (membrane retaining material with mol. wt. >25,000) to a vol. of 0.5 ml. The 5 toxins were concd. 14.8-112.2-fold.

L13 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1973:13556 CAPLUS
DOCUMENT NUMBER: 78:13556
TITLE: Purification and crystallization of Clostridium botulinum type C toxin
AUTHOR(S): Syuto, Bunei; Kubo, Shuichiro
CORPORATE SOURCE: Fac. Vet. Med., Hokkaido Univ., Sapporo, Japan
SOURCE: Jap. J. Vet. Res. (1972), 20(1-2), 19-30
CODEN: JJVRAE
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The toxin was pptd. from the culture by addn. of ZnCl2. The large mass of ppt. obtained was suspended in 0.6M Na2HPO4 at 30.degree., the suspension was stirred at room temp. for 2 hr, then left to stand overnight at 4.degree.. The insol. **compds**. and excess **phosphate** settled to the bottom, and clear supernatant contg. the toxin was obtained by decantatio. The toxin was then pptd. with (NH4)2SO4 at 34% satn. at 4.degree., dissolved in acetate-**phosphate buffer**, and chromatographed sequentially on columns of Sephadex G-75, DEAE-cellulose, and QAE Sephadex A-50 at pH 7.0. The eluate had a specific toxicity of 3.8 .times. 107 LD50/unit of absorbance at 277.5 m.mu.. The toxin was cryst. and dialyzed vs. satd. (NH4)2SO4 soln. by ultrafiltration. The cryst. toxin had a specific toxicity of 3.0 .times. 107 LD50/unit of absorbance at 277.5 m.mu. and weak hemagglutinin activity. It contained .gtoreq.2 components, which sepd. in acrylamide gel electrophoresis and agar-gel immunodiffusion.

L13 ANSWER 15 OF 20 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1971:472137 CAPLUS
DOCUMENT NUMBER: 75:72137
TITLE: Toxin production by naturally occurring levels of Clostridium botulinum in irradiated and nonirradiated seafood
AUTHOR(S): Nickerson, J. T. R.; Goldblith, S. A.
CORPORATE SOURCE: Massachusetts Inst. Technol., Cambridge, Mass., USA
SOURCE: U. S. At. Energy Comm. (1971), MIT-4049-2, 26

pp. Avail.: Dep. NTIS
From: Nucl. Sci. Abstr. 1971, 25(8), 16391
CODEN: XAERAK
DOCUMENT TYPE: Report
LANGUAGE: English

AB A total of 150 samples (450 individual portions) of com. produced cod and haddock fillets have been incubated and tested for **botulinum toxin**. Each sample consisted of ground and mixed cod or haddock fillets, packaged in polyethylene as 3 different 100-g portions. Among the 3 100-g portions which made up each sample, 1 received no further treatment, 1 was irradiated with .gamma.-rays at a dose level of 100 krad, and 1 was irradiated with .gamma.-rays at a dose level of 200 krad. As packaged the conditions in the fish portions were aerobic but doubtlessly changed to anaerobic as bacterial growth proceeded during incubation. All portions of all samples were incubated for 6 days at 70.degree.F, then extd. with cold gel-**phosphate buffer**. Portions of the trypsinized and nontrypsinized exts. were injected i.p. into mice (protected and nonprotected with botulinum antitoxin, types A, B, and E) and the mice were obsd. over a period of 96 hr for symptoms of botulism and death. All mice had been treated with antibiotics prior to injection. Among the 450 individual portions tested, only 1, a 200-krad treated portion, caused symptoms and death typical of botulism upon injection into mice. Because of various circumstances (time of death in animals protected with individual antitoxins, A, B, and E, and the symptoms exhibited by injected mice), it was concluded that this portion contained type A **botulinum toxin**. None of the portions treated with .gamma.-rays at a level of 100 krad and none of the untreated samples produced symptoms of botulism in mice when exts. were injected. The dose rate of the Mark II 60Co source was detd. This was done in such a manner that the same mass was present in the irradn. chamber as when fish fillets were irradiated in quantities of 20 lb (two 10 lb containers) and as the 100-g portions were irradiated for the expts. reported herein.

L13 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1971:97326 CAPLUS
DOCUMENT NUMBER: 74:97326
TITLE: Radiosensitivity of type E **botulinum toxin** and its protection by proteins, nucleic acids, and some related substances
AUTHOR(S): Miura, Toshiyuki; Sakaguchi, Sumiko; Sakaguchi, Genji; Miyaki, Komei
CORPORATE SOURCE: Dep. Food Res., Natl. Inst. Health, Tokyo, Japan
SOURCE: Proc. U. S. - Jap. Conf. Toxic Micro-Organisms, 1st (1970), Meeting Date 1968, 454-8. Editor(s): Herzberg, Mendel. GPO: Washington, D. C.

CODEN: 22XNAU
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Three prepns. of type E **botulinum toxin** of varying purity were irradiated with 60Co in 0.05M acetate or 0.2M **phosphate buffer** of pH 6.0. The D-values were .apprx.2.1 Mrad for the cell suspension, .apprx.0.21 Mrad for the cell ext., and .apprx.0.04 Mrad for the purified prepn. Tryptic activation did not change the radiosensitivity of the toxin except for the cell suspension. Serum albumin, casein, DNA, and RNA protected the purified and activated toxin against radiation detoxification; sugars or ascorbic acid exhibited little or no protection. S-contg., aromatic, or heterocyclic amino acids as well as purines showed protection similar to that of proteins. Preirradn. of amino acid solns. with 7.7 Mrad was without influence on the protecting effect, except the irradiated lysine, which was effective in some expts. Some amino acid derivs. like methionine sulfoxide, aminoethyl mercaptan or cadaverine were protective to different extents.

L13 ANSWER 17 OF 20 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1971:75322 CAPLUS
DOCUMENT NUMBER: 74:75322
TITLE: Toxin production by naturally occurring levels of Clostridium botulinum in irradiated and nonirradiated seafood
AUTHOR(S): Nickerson, John T. R.; Goldblith, Samuel A.
CORPORATE SOURCE: Massachusetts Inst. Tech., Cambridge, Mass., USA
SOURCE: U. S. At. Energy Comm. (1969), MIT-4049-2, 24 pp. Avail.: Dep. CFSTI
From: Nucl. Sci. Abstr. 1970, 24(11), 21331
CODEN: XAERAK
DOCUMENT TYPE: Report
LANGUAGE: English
AB Avail. Dep. CFSTI. From Nucl. Sci. Abstr. 1970, 24(11), 21331. A total of 150 samples (450 individual portions) of com. produced cod and haddock fillets were incubated and tested for **botulinum toxin**. Each sample consisted of ground and mixed cod or haddock fillets packaged in polyethylene as three, 100-g portions. One portion of each sample received no further treatment, one portion was irradiated with .gamma.-rays at a dose level of 100 krad and 1 portion was irradiated with .gamma.-rays at a dose level of 200 krad. All portions of all samples were incubated for 6 days at 70.degree.F, then extd. with cold gel-**phosphate buffer**. The trypsinized and nontrypsinized exts. were injected i.p. into mice, protected and not protected with botulinum antitoxins (types A, B, and E). All mice were treated with antibiotics prior to injection. The mice were studied for 96 hr for symptoms of botulism and death. Among 480 individual portions

tested only one, a 200-krad treated portion, produced symptoms and death typical of botulism. This was not an E or B type but probably was type A botulism. Since in neutral vegetable products periods >30 days at 50.degree.F would be required for type A C. botulinum to outgrow and produce toxin, there is doubt that any public health hazard exists in treating fish fillets with .gamma.-rays at a level of 200 krad. None of the portions treated with .gamma.-rays at 100 krad produced symptoms of botulism in mice when injected.

L13 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1969:85842 CAPLUS
DOCUMENT NUMBER: 70:85842
TITLE: Purification and molecular dissociation of the precursor of Clostridium botulinum type E toxin
AUTHOR(S): Kitamura, Masaru; Sakaguchi, Simiko; Sakaguchi, Genji
CORPORATE SOURCE: Nat. Inst. Health, Tokyo, Japan
SOURCE: Anaerobic Bact., Proc. Int. Workshop, 5th (1968), Meeting Date 1967, 213-22. Editor(s): Fredette, V.. Inst. Microbiol. Hyg. Montreal Univ.: Laval-des-Rapides, Can.
CODEN: 20QCAI
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The toxin of C. botulinum type E is formed as a nontoxic ribonucleoprotein (I) which can be extd. from the cells with 0.2M **phosphate buffer**, pH 6.0. The protein moiety is purified by pptn. of I by half-satd. (NH4)2SO4, chromatog. on CM-Sephadex C-50 (II) at pH 6.0 (0.02M acetate **buffer**), digestion with RNase, rechromatog. on II at pH 6.0 with a linear concn. gradient of NaCl in 0.02M acetate **buffer**, pptn. by half-satd. (NH4)2SO4, chromatog. on Sephadex G-200, and rechromatog. on II. The toxicity of the product for mice was 2-8 LD50/mg. N, but activation by trypsin raised this to 5-10 LD50/mg. N. The material appeared homogeneous on disk electrophoresis (pH 4) and on ultracentrifugation (pH 4.5 or 6.0, s20, W 11.3-12.3 S), but gave 2 distinct precipitin lines on immunodiffusion and 2 distinct zones on electrophoresis (cellulose acetate) at pH 7. Ultracentrifugation at pH 8 (0.05M Veronal **buffer**) gave a single major band, s20, W 7.3 S. Starch-gel electrophoresis at pH 8 (0.05M Veronal **buffer**) gave partial sepn. into anodic and cathodic peaks; only the latter gave active toxin after treatment with trypsin.

L13 ANSWER 19 OF 20 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1968:46431 CAPLUS
DOCUMENT NUMBER: 68:46431
TITLE: Chromatographic isolation of hemagglutinin-free neurotoxin from crystalline toxin of Clostridium botulinum type A

AUTHOR(S): DasGupta, Bibhuti R.; Boroff, Daniel A.
CORPORATE SOURCE: Albert Einstein Med. Center, Philadelphia, Pa., USA
SOURCE: Biochim. Biophys. Acta (1967), 147(3), 603-5
CODEN: BBACAQ
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cryst. toxin in 0.025 M **phosphate** (I) **buffer** was applied to a DEAE-cellulose column equilibrated with the **buffer**, and eluted with a linear gradient of I. Three distinct peaks plus a trace 4th peak were eluted. The 1st (14.6% of the total eluted protein) was highly toxic, and showed no hemagglutinating activity. The next 2 strongly agglutinated red blood cells. The 1st peak was the .alpha. fraction previously obtained with Tris-HCl **buffer** chromatog. (loc. cit.). It was possible to sep. the .alpha. fraction by a 2nd, simpler procedure employing I **buffer**, without application of a gradient elution. The purification on DEAE-cellulose appeared to be as good with I as with Tris-HCl **buffer**. Isolation of the hemagglutinin-free neurotoxin by elution with 0.05M gave higher yields of this fraction than did elution with 0.025M I or Tris-HCl **buffer**. Substitution of Cl- with I did not appear to alter the resolution pattern of cryst. toxin or the neurotoxin. The fraction showed chromatog. homogeneity in both I and Tris-HCl **buffer**.

L13 ANSWER 20 OF 20 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1968:20941 CAPLUS
DOCUMENT NUMBER: 68:20941
TITLE: Demonstration of bacterial toxins in foodstuffs by means of immunofluorescence
AUTHOR(S): Riemann, Hans
CORPORATE SOURCE: Sch. of Vet. Med., Univ. of California, Davis, Calif., USA
SOURCE: Nord. Veterinaermed. (1967), 19(4), 188-94
CODEN: NOVTAV
DOCUMENT TYPE: Journal
LANGUAGE: Danish

AB Staphylococcal enterotoxin B antitoxin, obtained from rabbits, was conjugated with fluorescein isothiocyanate and purified on DEAE-cellulose and Sephadex columns. The conjugate was adsorbed to nontoxin-producing staphylococcal strains and purified as Sephadex. To avoid false neg. results due to extracellular localization of toxin, the conjugate and culture, after incubation at 30.degree. for 30 min. and at 20.degree. for 4 hrs., were filtered through a 0.22-.mu. pore filter plus Whatman No. 1 filter paper. Direct preparates were prepd. by growing cultures on dialysis membranes mounted on blood-agar. The preparate was freeze-dried and colored by incubation with conjugate at 37.degree.. With these methods 1

.gamma. toxin/ml. sample was detected. In a quant. modification, antiserum and agar were mixed (50:50) and poured into small glass tubes. Test soln. was pipetted on the gel and after 1-7 days incubation, the amt. of toxin was estd., being related to the distance between the surface and the line of pptn. With this method 4 .gamma./ml. were detectable after 8 days and 8 .gamma./ml. after 1 day. The toxin was identified by gel-diffusion technique. These methods were used for detn. of toxin in various foods. It was found that 1-10 .gamma. toxin was formed per g. ham on anaerobic storage for 8-13 days at room temp. The amt. of toxin formed varied according to pH and salt concn. At pH 6.9 and NaCl concn. 10-12 g./100 ml. and pH 5.1 and NaCl concn. 4 g./100 ml. both totally inhibited production of toxin. Com. Clostridium botulinum E antiserum was purified by pptn. with (NH4)2SO4 and chromate on Sephadex and in two steps adsorbed to nontoxin-producing and toxin-producing C. botulinum E. Com. rabbit antihorse serum .gamma.-globulin, conjugated with fluorescein isothiocyanate was dialyzed against a **phosphate buffer** and chromatographed on a DEAE-cellulose column. Preparates were incubated with antitoxin for 0.5-1 hr. at 37.degree. and again under the same conditions with rabbit antihorse serum. Neither nontoxic strain E nor strain A or B or pseudobotulinum E from toxic cultures of strain E showed fluorescence with reagent. Toxic cultures of strain E showed no fluorescence when tested against antitoxin A or B. Incubations of ham showed, when tested on mice, that toxin was produced when the salt concn. decreased under 2.5 g./100 ml. H2O; these expts., however, were neg. to the fluorescence being described.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, TOXLIT, TOXLINE, PHIC, PHIN' ENTERED AT 14:19:29 ON 26 SEP 2000)

L14 44 S L13
L15 26 DUP REM L14 (18 DUPLICATES REMOVED)

L15 ANSWER 1 OF 26 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-505733 [45] WPIDS
DOC. NO. CPI: C2000-151733
TITLE: New spectrofluorometrically detectable luminescent **composition**, useful for detecting e.g. vitamins, hormones, pharmaceuticals, drugs, pesticides, proteins or nucleic acids.
DERWENT CLASS: B02 B04 D16
INVENTOR(S): LEIF, R C; VALLARINO, L
PATENT ASSIGNEE(S): (LEIF-I) LEIF R C; (VALL-I) VALLARINO L
COUNTRY COUNT: 21
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

WO 2000042048 A1 20000720 (200045)* EN 94
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA CH DE FI GB JP US

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000042048 A1		WO 2000-US1211	20000118

PRIORITY APPLN. INFO: US 2000-116316 20000118; US 1999-116316 19990119

AN 2000-505733 [45] WPIDS

AB WO 200042048 A UPAB: 20000918

NOVELTY - A novel spectrofluorimetrically detectable luminescent **composition** comprises water, a micelle-producing amount of at least one surfactant, at least one energy transfer acceptor lanthanide element macrocycle compound (EALM) having an emission spectrum peak of 500-950 nm, and at least one energy transfer donor compound of yttrium or a 3-valent lanthanide element having atomic number 59-71.

DETAILED DESCRIPTION - A novel spectrofluorimetrically detectable luminescent **composition** comprises water, a micelle-producing amount of at least one surfactant, at least one energy transfer acceptor lanthanide element macrocycle compound (EALM) (at least 1 x 10-10 moles/liter) having an emission spectrum peak of 500-950 nm, and a luminescence-enhancing amount of at least one energy transfer donor compound of yttrium or a 3-valent lanthanide element having atomic number 59-71, provided that the lanthanide element of the macrocycle compound and the lanthanide element of the energy transfer donor compound are not identical.

An INDEPENDENT CLAIM is also included for a method for analysis of a sample containing or suspected of containing at least one analyte, frequently a biologically active compound, the method comprising:

(a) contacting the sample with a functionalized complex of a metal M, where M is a metal ion selected from a lanthanide having atomic number 57-71, and actinide having atomic number 89-103, and yttrium (III) having atomic number 39; in a reaction medium under binding conditions, whereby the analyte when present either interacts with the complex to form a conjugate or competes for interaction with a binding material specific for interaction with the complex and with the analyte;

(b) adding to the reaction medium a luminescence-enhancing amount of at least one energy transfer donor compound of yttrium or a 3-valent lanthanide element having atomic number 59-71, provided that the lanthanide element of the macrocycle compound and a lanthanide element of the energy transfer donor compound are not

identical;

(c) subjecting the reaction medium to excitation energy in the range of 200-400 nm, whereby enhanced luminescence in the range of 500-950 nm is generated;

(d) monitoring the luminescence of the reaction medium to measure in the sample: (i) the presence and/or concentration of the conjugate; (ii) the presence and/or concentration of the product of the interaction of the complex with the binding material; and/or (iii) the presence and/or concentration of the product of the interaction of the conjugate with the binding material.

USE - The method can be used for the detection of analytes such as vitamins, vitamin precursors, and vitamin metabolites including retinal, vitamin K, cobalamin, biotin folate; hormones and related compounds including steroid hormones including estrogen, corticosterone, testosterone, ecdysone; amino acid derived hormones including thyroxine, epinephrine; prostaglandins; peptide hormones including oxytocin, somatostatin; pharmaceuticals including aspirin, penicillin, hydrochlorothiazide; nucleic acid constituents including natural and synthetic nucleic acid bases including cytosine, thymine, adenine, guanine, uracil, derivatives of the bases including 5-bromouracil, natural and synthetic nucleosides and deoxynucleosides including 2-deoxyadenosine, 2-deoxycytidine, 2-deoxythymidine, 2-deoxyguanosine, 5-bromo-2-deoxyuridine, adenosine, cytidine, uridine, guanosine, 5-bromouridine; drugs of abuse including cocaine, tetrahydrocannabinol; histological stains including fluorescein, DA PI, pesticides including digitoxin; and miscellaneous haptens including diphenylhydantoin, quinidine, RDX; polyaminoacids, polypeptides, proteins, polysaccharides, nucleic acids, glycosaminoglycans, glycoproteins, ribosomes, and proteins and their combinations including albumins, globulins, hemoglobin, staphylococcal protein A, alpha-feto-protein, retinal-binding protein, avidin, streptavidin, C-reactive protein, collagen, keratin; immunoglobulins including IgG, IgM, AgA, IgE; hormones including lymphokines, follicle stimulating hormone, and thyroid stimulating hormone; enzymes including trypsin, peptide, reverse transcriptases; cell surface antigens on T- and B-lymphocytes, i.e. CD-4, CD-8, CD-20 proteins, and the leukocyte cell surface antigens; blood group antigens including A, B and Rh; major histocompatilibity antigens both of class 1 and 2; hormone receptors including estrogen receptor, progesterone receptor, and glucocorticoid receptor; cell cycle associated proteins including protein kinases, cyclins, PCNA, p53; antigens associated with cancer diagnosis and therapy including BRCA(s) carcinoembryonic antigen, HPV 16, HPV 18, MDR, c-neu, tumor suppressor proteins, p53 and retinalblastoma; apoptosis related markers including annexin V, bak, bcl-2, fas caspases, nuclear matrix protein, cytochrome c, nucleosome; toxins including cholera toxin, diphtheria toxin, **botulinum toxin**, snake venom toxins, tetrodotoxin, saxitoxin; lectins including concanavalin, wheat germ agglutinin, soy bean agglutinin; polysialic

acids including chitin; polynucleotides including RNAs including segments of the HIV genome, human hemoglobin A, mRNA, DNAs including chromosome specific sequences, centromeres, telomere specific sequences, single copy sequences from normal tissues, or single copy sequences from tumors (claimed). The **compositions** can also be used in analytical cytology, histological staining and imaging processing.

ADVANTAGE - The **compositions** do not require the prior dissociation of the luminescence-enhanced complex before measuring its emission spectrum, and do not require time-gated detection systems. Using the method, 2 different analytes can be measured in the presence of one another.

Dwg.0/15

L15 ANSWER 2 OF 26 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-271251 [23] WPIDS
DOC. NO. CPI: C2000-082761
TITLE: Stable liquid pharmaceutical **botulinum toxin formulation**, useful for treating spasticity due to stroke, spinal cord injury, closed head trauma, cerebal palsy, multiple sclerosis, or Parkinson's disease.
DERWENT CLASS: B04
INVENTOR(S): HIRTZER, P; MOYER, E
PATENT ASSIGNEE(S): (ELAN-N) ELAN PHARM INC
COUNTRY COUNT: 83
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000015245	A2	20000323	(200023)*	EN	34

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW

AU 9958214	A	20000403 (200034)	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000015245	A2	WO 1999-US20912	19990909
AU 9958214	A	AU 1999-58214	19990909

FILING DETAILS:

PATENT NO	KIND	PATENT NO

AU 9958214 A Based on WO 200015245

PRIORITY APPLN. INFO: US 1998-99870 19980911
AN 2000-271251 [23] WPIDS
AB WO 200015245 A UPAB: 20000516
NOVELTY - A stable liquid pharmaceutical **botulinum toxin formulation** (I), comprising a **buffer** giving a pH range of 5 to 6 and isolated **botulinum toxin**, stable at a temperature of 0 to 30 deg. C for at least 1 year, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method of treating a patient requiring inhibition of cholinergic input to a muscle, gland, or organ comprising administering (I).

ACTIVITY - Relaxant; cerebroprotective; neuroprotective; antiparkinsonian; analgesic; antimigraine; antiasthmatic.

Twenty-eight patients with a mean age of 50.9 with a confirmed diagnosis of cervical dystonia, received injections of **botulinum toxin** Type B **formulation** into 2-4 superficial neck and shoulder muscles with escalating doses (up to 1.5 fold per successive session) over time. Clinical benefit was assessed using the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS)-Severity test, with 25% reduction in score considered an improvement. Patients participated in the study from 28 to 177 days with a mean time in the study of 71.9 days. Patients were treated with 1 to 3 doses of **formulation**. Cumulative doses ranged from 1430 U to 12000 U, with individual doses ranging from 300 U to 12000 U. For purposes of clinical assessment, 4 dose groups were defined: 100-800 U (Group A), 900-2399 U (Group B), 2400-5999 U (Group C), and 6000-12000 U (Group D). The length of time between dosing sessions ranged as follows: Group A, 13-101 days; Group B, 14-113 days; Group C, 29-177 days; and Group D, 28-177 days. Mean baseline scores were similar in all patients in all treatment groups, and all 4 groups experienced a mean decrease in score (improvement) during the study. Overall, mean percent improvement from baseline and mean response ratio for severity score was greatest in Groups C and D during the study. Measures of mean maximum improvement, mean maximum percent improvement and mean maximum response ratio were greater for the two higher dose groups (8.1 and 6.8 against 2.1 and 3.6 for maximum improvement). The percentage of patients responding to treatment was greater for the two higher dose groups (80 and 78% for C and D, respectively compared to 0 and 27% for A and B, respectively). The results therefore showed a dose-dependent response to botulinum B toxin **formulations**.

MECHANISM OF ACTION - (I) inhibits cholinergic input into muscles, glands and organs.

USE - The **composition** is useful for treating spasticity (due to stroke, spinal cord injury, closed head trauma,

cerebal palsy, multiple sclerosis, or Parkinson's), blepharospasm, strabismus, hemifacial spasm, dystonia, otitis media, spastic colitis, anismus, urinary detrusor-sphincter dyssynergia, jaw-clenching, and curvature of the spine. (I) is also useful for treatment of myofascial pain, headache associated with migraine, vascular disturbances, neuralgia, neuropathy, arthrotos pain, back pain, hyperhydrosis, rhinnorhea, asthma, excessive salivation, and excessive stomach acid secretion.
Dwg.0/0

L15 ANSWER 3 OF 26 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000272711 EMBASE
TITLE: Botox and dysport are distinct (multiple letters).
AUTHOR: Madalinski M.; Thumshirn M.
CORPORATE SOURCE: M. Madalinski, ul. Kosciuszki 101-7, 80-421 Gdansk, Poland. m.h.madalinski@pro.onet.pl
SOURCE: Endoscopy, (2000) 32/6 (502-503).
Refs: 0
ISSN: 0013-726X CODEN: ENDCAM
COUNTRY: Germany
DOCUMENT TYPE: Journal; Letter
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
048 Gastroenterology
LANGUAGE: English

L15 ANSWER 4 OF 26 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 1
ACCESSION NUMBER: 1999:334364 BIOSIS
DOCUMENT NUMBER: PREV199900334364
TITLE: Detection of sparse **botulinum toxin** A binding sites using fluorescent latex microspheres.
AUTHOR(S): Crosland, Richard D. (1); Canziani, Gabriela A.
CORPORATE SOURCE: (1) Toxinology Division, United States Army Medical Research Institute of Infectious Diseases, Frederick, MD, 21702 USA
SOURCE: Journal of Histotechnology, (June, 1999) Vol. 22, No. 2, pp. 113-115.
ISSN: 0147-8885.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The most potent toxins known are produced by strains of Clostridium botulinum. To paralyze the vertebrate neuromuscular junction, the toxins bind selectively to nerve endings, translocate into the presynaptic terminal, and hydrolyze proteins of the exocytotic apparatus, thus inhibiting the release of acetylcholine. Our goal was to develop a convenient, reliable technique to detect specific

binding of **botulinum toxin** A to its targets, a technique that could be easily modified to detect the binding sites of other ligands as well. Our method utilized fluorescent latex microspheres and is theoretically capable of detecting a single binding site at the light microscopic level. Nonspecific binding sites on 7-mum thick sections of unfixed, cryosectioned mouse diaphragm were first blocked with 20% goat serum in **phosphate-buffered** saline (GS/PBS). We incubated the diaphragm for 1 hr at 22degree with various concentrations of **botulinum toxin** A in GS/PBS, followed by incubation with rabbit anti-**botulinum toxin** A antiserum, biotin-labeled goat anti-rabbit antibody, and finally avidin-labeled, 0.03 mum diameter, fluorescent latex microspheres. As expected, binding was localized to the area of the neuromuscular junction. Binding was also observed in association with axons innervating some junctions. We could detect binding on diaphragms that were exposed to as little as 10 pM **botulinum toxin** A, which is in the low range of effective in vitro doses that block neuromuscular transmission. This is a convenient, sensitive, and specific technique for detecting **botulinum toxin** A binding sites that is easily modifiable for the detection of binding sites of other ligands as well.

L15 ANSWER 5 OF 26 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 2
ACCESSION NUMBER: 1998:261992 BIOSIS
DOCUMENT NUMBER: PREV199800261992
TITLE: A comparison of the spread of three **formulations** of botulinum neurotoxin A as determined by effects on muscle function.
AUTHOR(S): Dodd, S. L. (1); Rowell, B. A.; Vrabas, I. S.; Arrowsmith, R. J.; Weatherill, P. J.
CORPORATE SOURCE: (1) Coll. Health Human Performance 27 FLG, Univ. Florida, Gainesville, FL 32611 USA
SOURCE: European Journal of Neurology, (March, 1998) Vol. 5, No. 2, pp. 181-186.
ISSN: 1351-5101.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The purpose of these experiments was to compare the spread of three **formulations** of botulinum neurotoxin A. A gelatin/**phosphate buffer** (C), DysportR (D (0.5 U), BotoxR (B (0.167 U)), or a purified preparation of botulinum neurotoxin A (Bont A) (BA (0.5 U)) was injected into the tibialis anterior of male, Wistar rats. After 4 days, the adjacent extensor digitorum longus muscle was isolated in situ and the nerve was maximally stimulated to determine contractile properties and the rate of fatigue. There were no differences in body or muscle weights between any of the groups after 4 days of treatment. Maximal twitch and tetanic tensions were decreased apprxeq 25% ($p < 0.05$) in all

treatment groups compared to C. In addition, rate of tension development was significantly less in all treatment groups compared to C but one-half relaxation time and time to peak tension were not different between any groups. Fatigue of the muscle was significantly faster in all groups compared to C but there was no difference between treatment groups. These data indicated that **botulinum toxin** A injected intramuscularly was likely to spread to adjacent muscles but that the spread was not different between the three **formulations** tested. The effect of the spread ranged from a slight to a severe reduction in maximal tension but this did not occur in all animals studied.

L15 ANSWER 6 OF 26 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 95274849 MEDLINE
DOCUMENT NUMBER: 95274849
TITLE: Adsorption of **botulinum toxin** to activated charcoal with a mouse bioassay [published erratum appears in Ann Emerg Med 1995 Aug;26(2):152].
AUTHOR: Gomez H F; Johnson R; Guven H; McKinney P; Phillips S; Judson F; Brent J
CORPORATE SOURCE: Rocky Mountain Poison and Drug Center, Denver General Hospital, Denver Health and Hospitals, University of Colorado Health Sciences Center, USA.
SOURCE: ANNALS OF EMERGENCY MEDICINE, (1995 Jun) 25 (6) 818-22.
Journal code: 4Z7. ISSN: 0196-0644.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199508
AB STUDY OBJECTIVE: We evaluated the effectiveness of activated charcoal (AC) in adsorbing Clostridium botulinum type A toxin using a mouse bioassay. DESIGN: Prospective, blinded, randomized, controlled animal study. SETTING: Animal care facility. PARTICIPANTS: One hundred forty Swiss/Webster ND-4 strain mice. INTERVENTION: Food contaminated with type A **botulinum toxin** was homogenized in a **phosphate**/gel **buffer** (pH 6.2). The concentrate was diluted by factors of 1:10, 1:50, and 1:100. AC was added to aliquots of the dilutions to a 20% final concentration. The samples were centrifuged, supernatant was removed, and separate groups of mice were injected intraperitoneally with .5 mL of each dilution (those treated with AC and controls untreated with AC). The animals were then observed over 5 days for signs of botulism. RESULTS: None of the 60 animals injected intraperitoneally with dilutions treated with AC was observed to have any signs of botulism. In contrast, deaths were observed in 10 of 20, 9 of 20 and 4 of 20 mice injected with untreated dilutions of 1:100, 1:50, and 1:10, respectively (P <

.004). CONCLUSION: In this model, treatment of **botulinum toxin** with AC before administration resulted in greatly reduced morbidity and mortality.

L15 ANSWER 7 OF 26 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1994-127999 [16] WPIDS
DOC. NO. CPI: C1994-058949
TITLE: **Compsn** comprising active **botulinum toxin** type A free from sodium chloride - with higher activity of gross amts of toxin, esp in presence of stabiliser and lower pH.
DERWENT CLASS: B04
INVENTOR(S): GOODNOUGH, M C; JOHNSON, E A; SCHANTZ, E J
PATENT ASSIGNEE(S): (WISC) WISCONSIN ALUMNI RES FOUND
COUNTRY COUNT: 18
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 593176	A2	19940420	(199416)*	EN	6
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE					
JP 06192118	A	19940712	(199432)		6
EP 593176	A3	19950301	(199541)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 593176	A2	EP 1993-307656	19930928
JP 06192118	A	JP 1993-263081	19930928
EP 593176	A3	EP 1993-307656	19930928

PRIORITY APPLN. INFO: US 1992-951604 19920928
AN 1994-127999 [16] WPIDS
AB EP 593176 A UPAB: 19940608
Pharmaceutical **compsn.** consisting of lyophilised active **botulinum toxin** type A, free of sodium chloride, is new.

In (a) a protein stabiliser, esp. serum albumin, is present and the **buffer** has pH 5.0-6.8. Most pref., the prod. contg. serum albumin stabiliser, has pH 6.2-6.8, and is free of inactive toxin.

USE/ADVANTAGE - Some patients have developed antibodies to the toxin, rendering it ineffective. The presence commercial process for toxin prodn., in lyophilising with NaCl and opt. human serum albumin (HSA), results in inactivation of about 80-90% of the toxin, and it is suggested that this acts as a toxoid to generate antibodies.

Dwg.0/0

L15 ANSWER 8 OF 26 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 89330489 MEDLINE
DOCUMENT NUMBER: 89330489
TITLE: Molecular topography and secondary structure comparisons of botulinum neurotoxin types A, B and E.
AUTHOR: Singh B R; DasGupta B R
CORPORATE SOURCE: Food Research Institute, University of Wisconsin, Madison 53706.
CONTRACT NUMBER: NS17742 (NINDS)
NS24545 (NINDS)
SOURCE: MOLECULAR AND CELLULAR BIOCHEMISTRY, (1989 Mar 16) 86 (1) 87-95.
Journal code: NGU. ISSN: 0300-8177.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198911
AB Botulinum neurotoxin (NT) serotypes A, B and E differ in microstructure and biological activities. The three NTs were examined for secondary structure parameters (alpha-helix, beta-sheet, beta-turn and random coil content) on the basis of circular dichroism; degree of exposed Tyr residues (second derivative spectroscopy) and state of the Trp residues (fluorescence and fluorescence quantum yield). The proteins are high in beta-pleated sheet content (41-44%) and low in alpha-helical content (21-28%). About 30-36% of the amino acids are in random coils. The beta-sheet contents in the NTs are similar irrespective of their structural forms (i.e. single or dichain forms) or level of toxicity. About 84%, 58% and 61% of Tyr residues of types A, B, and E NT, respectively, were exposed to the solvent (pH 7.2 **phosphate buffer**). Although the fluorescence emission maximum of Trp residues of type B NT was most blue shifted (331 nm compared to 334 for types A and E NT, and 346 nm for free tryptophan) the fluorescence quantum yields of types A and B were similar and higher than type E. In general the NTs have similar secondary (low alpha-helix and high beta-sheets) and tertiary (exposed tyrosine residues and tryptophan fluorescence quantum yield) structures. Within this generalized picture there are significant differences which might be related to the differences in their biological activities.

L15 ANSWER 9 OF 26 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 89155384 MEDLINE
DOCUMENT NUMBER: 89155384
TITLE: Studies on the irradiation of toxins of Clostridium botulinum and Staphylococcus aureus.

Searcher : Shears 308-4994

AUTHOR: Rose S A; Modi N K; Tranter H S; Bailey N E; Stringer M F; Hambleton P
CORPORATE SOURCE: Campden Food and Drink Research Association, Gloucestershire, UK.
SOURCE: JOURNAL OF APPLIED BACTERIOLOGY, (1988 Sep) 65 (3) 223-9.
Journal code: HDJ. ISSN: 0021-8847.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198906

AB The effects of irradiation of Clostridium botulinum neurotoxin type A (BNTA) and staphylococcal enterotoxin A (SEA) in gelatin **phosphate buffer** and cooked mince beef slurries were investigated. Estimation of toxins by immunoassays showed that in **buffer**, toxins were destroyed by irradiation at 8.0 kGy; in mince slurries however, 45% of BTNA and 27-34% of SEA remained after this level of irradiation. At 23.7 kGy, over twice the dose of irradiation proposed for legal acceptance in the UK, 15% of BNTA and 16-26% of SEA still remained. Increasing concentrations of mince conferred increased protection against the effect of irradiation on both toxins. The biological activity of BNTA was more sensitive to irradiation than the immunological activity. Staphylococcal enterotoxin was more resistant to irradiation than BNTA. Irradiation should therefore only be used in conjunction with good manufacturing practices to prevent microbial proliferation and toxin production prior to irradiation.

L15 ANSWER 10 OF 26 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 88278849 MEDLINE
DOCUMENT NUMBER: 88278849
TITLE: Purification of Clostridium botulinum type G progenitor toxin.
AUTHOR: Nukina M; Mochida Y; Sakaguchi S; Sakaguchi G
CORPORATE SOURCE: Public Health Research Institute of Kobe City, Hyogo, Japan.
SOURCE: ZENTRALBLATT FUR BAKTERIOLOGIE, MIKROBIOLOGIE, UND HYGIENE. SERIES A, MEDICAL MICROBIOLOGY, INFECTIOUS DISEASES, VIROLOGY, PARASITOLOGY, (1988 Apr) 268 (2) 220-7.
Journal code: Y55. ISSN: 0176-6724.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198810

AB Clostridium botulinum type G cultured for 6 days at 30 degrees C in proteose peptone-yeast extract-glucose medium produced toxin of 1.3

x 10(4) LD50/ml. The toxin was precipitated at pH 4.0, extracted with 0.2 M **phosphate buffer**, pH 6.0, and activated with trypsin. Sonic treatment and trypsinization of the residual precipitate released additional toxin, the toxicity of which corresponded to that detected in whole culture. Activated toxin obtained from the first extract and that from the residual precipitate were combined and purified by salting out, acid precipitation, gel filtration on Sephadex G-200, chromatography on SP-Sephadex, and a second gel filtration on Sephadex G-200. The yield of purified toxin from 10 liters of culture was 22.9 mg an 1.1 X 10(8) mouse ip LD50 with a specific toxicity of 3.0 X 10(7) mouse ip LD50/mg nitrogen. The molecular weight of the toxin was about 500,000, corresponding to that of L toxin of the other types. No M nor LL toxin was detected.

L15 ANSWER 11 OF 26 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 88132780 MEDLINE
DOCUMENT NUMBER: 88132780
TITLE: Simplified purification method for Clostridium botulinum type E toxin.
AUTHOR: Gimenez J A; Sugiyama H
CORPORATE SOURCE: Food Research Institute, University of Wisconsin, Madison 53706.
SOURCE: APPLIED AND ENVIRONMENTAL MICROBIOLOGY, (1987 Dec) 53 (12) 2827-30.
Journal code: 6K6. ISSN: 0099-2240.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198805
AB Clostridium botulinum type E toxin was purified in three chromatography steps. Toxin extracted from cells was concentrated by precipitation and dissolving in a small volume of **citrate buffer**. When the extract was chromatographed on DEAE-Sephadex without RNase or protamine treatment, the first protein peak had most of the toxin but little nucleic acid. When the toxic pool was applied to a carboxymethyl Sepharose column, toxin was recovered in the first protein peak in its bimolecular complex form. The final chromatography step at 4 degrees C on a DEAE-Sephacel column at a slightly alkaline pH purified the toxin (Mr, 145,000) by separating the nontoxic protein from the complex. At least 1.5 mg of pure toxin was obtained from each liter of culture, and the toxicity was 6 X 10(7) 50% lethal doses per mg of protein. These values are significantly higher than those previously reported.

L15 ANSWER 12 OF 26 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 86220811 MEDLINE

DOCUMENT NUMBER: 86220811
TITLE: TLC immunostaining characterization of Clostridium botulinum type A neurotoxin binding to gangliosides and free fatty acids.
AUTHOR: Takamizawa K; Iwamori M; Kozaki S; Sakaguchi G; Tanaka R; Takayama H; Nagai Y
SOURCE: FEBS LETTERS, (1986 Jun 9) 201 (2) 229-32.
Journal code: EUH. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198609
AB The receptor structure of Clostridium botulinum neurotoxin type A was analysed by TLC immunostaining. GQ1b was found to be the most potent receptor, and the neurotoxin also bound to GT1b and GD1a, but not to GM3, GM2, GM1, GD3, GD1b and GT1a. Optimum binding of neurotoxin to the ganglioside appeared in 0.01 M **phosphate buffer** (pH 7.2) containing 0.2% NaCl. Higher and lower NaCl concentrations diminished neurotoxin binding to the ganglioside. In addition, the neurotoxin was able to bind to free fatty acids. Maximum binding was observed on stearic acid and neurotoxin binding to free fatty acids was not affected by NaCl concentration.

L15 ANSWER 13 OF 26 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 81168134 MEDLINE
DOCUMENT NUMBER: 81168134
TITLE: Separation and characterization of heavy and light chains from Clostridium botulinum type C toxin and their reconstitution.
AUTHOR: Syuto B; Kubo S
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1981 Apr 25) 256 (8) 3712-7.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198108
AB Clostridium botulinum type C toxin consists of a heavy and a light chain with molecular weights of 98,000 and 53,000, respectively, which are linked by one disulfide bond. The two components were separated from each other by quaternary aminoethyl Sephadex A-50 column chromatography by stepwise elution with NaCl in 27.5 mM borax-45 mM sodium dihydrogen **phosphate buffer**, pH 8.0, containing 5% 2-mercaptoethanol at 0 degrees C. The purified components had different amino acid **compositions** and antigenicities, and the toxicity of the toxin was neutralized completely by either anti-heavy chain Fab or anti-light chain Fab.

the two components could be reconstituted to form an active molecule with recovered toxicity which varied according to the method used. Maximum recovery was obtained in a system in which the intersubunit S--S bond was first formed in the presence of high concentration of neutral salts, after which the concentration of salt was gradually decreased. The reconstituted preparation was highly toxic and had the same properties as the parental toxin on chromatography, sodium dodecyl sulfate-polyacrylamide gel electrophoresis, and immunodiffusion. By the use of three perturbants, the fractions of exposed tryptophans and tyrosines of the preparation were found to be almost the same as that of the parental toxin.

L15 ANSWER 14 OF 26 MEDLINE
ACCESSION NUMBER: 81081893 MEDLINE
DOCUMENT NUMBER: 81081893
TITLE: [Production of a homogeneous Cl. botulinum type B neurotoxin].
Poluchenie gomogennogo neirotksina Cl. botulinum tipa B.
AUTHOR: Saprykina T P; Kliucheva V V; Blagoveshchenskii V A; Mironova M V
SOURCE: ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII, (1980 Sep) (9) 86-91.
Journal code: Y9O. ISSN: 0049-8726.
PUB. COUNTRY: USSR
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198104
AB The method for obtaining the neurotoxin, or alpha-fraction of the toxin, of Cl. botulinum, type B, is described. In accordance with this method, the toxin was precipitated three times with hydrochloric acid in the isoelectric zone with subsequent extraction with **phosphate** (pH 6.8) and **citrate-phosphate** (pH 5.6) **buffers**, then fractionated in columns with DEAE cellulose (pH 5.6), DEAE Sephadex A-50 (pH 7.2) and Sephadex G-200 (pH 7.2). The homogeneous neurotoxin preparations with molecular weights ranging from 145,000 to 160,000 and having the isoelectric point at pH 5.5 and toxicity 5.0--10.0 x 10(7) Dlm per 1 mg protein were obtained.

L15 ANSWER 15 OF 26 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 81005398 EMBASE
DOCUMENT NUMBER: 1981005398
TITLE: Obtaining homogeneous neurotoxin of Cl. botulinum, type B.
AUTHOR: Saprykina T.P.; Klyucheva V.V.; Blagoveshchensky V.A.; Mironova M.V.
CORPORATE SOURCE: Inst. Epidemiol. Mikrobiol., AMN SSSR, Moscow, Russia

SOURCE: Zhurnal Mikrobiologii Epidemiologii i Immunobiologii, (1980) 57/9 (86-91).
CODEN: ZMEIAV
COUNTRY: Russia
DOCUMENT TYPE: Journal
FILE SEGMENT: 004 Microbiology
037 Drug Literature Index
LANGUAGE: Russian
SUMMARY LANGUAGE: English

AB The method for obtaining the neurotoxin, or .alpha.-fraction of the toxin, of Cl. botulinum, type B, is described. In accordance with this method, the toxin was precipitated three times with hydrochloric acid in the isoelectric zone with subsequent extraction with **phosphate** (pH 6.8) and **citrate-phosphate** (pH 5.6) **buffers**, then fractionated in columns with DEAE cellulose (pH 5.6), DEAE Sephadex A-50 (pH 7.2) and Sephadex G-200 (pH 7.2). The homogeneous neurotoxin preparations with molecular weights ranging from 145,000 to 160,000 and having the isoelectric point at pH 5.5 and toxicity 5.0-10.0 x 107 Dlm per 1 mg protein were obtained.

L15 ANSWER 16 OF 26 TOXLIT
ACCESSION NUMBER: 1981:11230 TOXLIT
DOCUMENT NUMBER: CA-094-042392A
TITLE: Isolation and properties of highly purified type F Clostridium **botulinum toxin**.
AUTHOR: Uvarova RN; Reshetnikova LN; Ispolatovskaya MV; Bulatova TI
CORPORATE SOURCE: Inst. Epidemiol. Mikrobiol., Moscow
SOURCE: Zh. Mikrobiol., Epidemiol. Immunobiol, (1980). No. 11, pp. 42-6.
CODEN: ZMEIAV.
FILE SEGMENT: CA
LANGUAGE: Russian
OTHER SOURCE: CA 94:42392
ENTRY MONTH: 198103

AB The steps involved in the isolation of C. **botulinum toxin** were initial pptn. with (NH4)2SO4 or Na hexametaphosphate after cultivation of the culture for 4 days at 28.degree., ultrafiltration through amicon membrane, gel filtration on 2 sephadex G-100 columns and elution with pH 5.6 Na **phosphate-phosphate buffer**, chromatog. on DEAE-cellulose, dialysis in a pH 4.2 acetate **buffer** contg. 0.1 M NaCl, chromatog. on SP-sephadex (C-50), repeating of dialysis, ultrafiltration and then gel filtration on sephadex G-200, and finally dialysis and chromatog. on DEAE-cellulose. The activity of the purified toxin ranged 1.5-4 .times. 107 (min. LD)/mg protein and had a mol. wt. of 50,000 daltons.

L15 ANSWER 17 OF 26 TOXLINE
ACCESSION NUMBER: 1981:21886 TOXLINE
DOCUMENT NUMBER: TOXBIB-81-081893
TITLE: Production of a homogeneous Cl. botulinum type B neurotoxin.
AUTHOR: Saprykina T P; Kliucheva V V; Blagoveshchenskii V A; Mironova M V
SOURCE: ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII, (1980). Zh Mikrobiol Epidemiol Immunobiol, ISS 9, 1980, P86-91.
Journal code: Y9O. ISSN: 0049-8726.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: TOXBIB
LANGUAGE: Russian
OTHER SOURCE: MEDLINE 81081893
ENTRY MONTH: 198104
AB The method for obtaining the neurotoxin, or alpha-fraction of the toxin, of Cl. botulinum, type B, is described. In accordance with this method, the toxin was precipitated three times with hydrochloric acid in the isoelectric zone with subsequent extraction with **phosphate** (pH 6.8) and **citrate-phosphate** (pH 5.6) **buffers**, then fractionated in columns with DEAE cellulose (pH 5.6), DEAE Sephadex A-50 (pH 7.2) and Sephadex G-200 (pH 7.2). The homogeneous neurotoxin preparations with molecular weights ranging from 145,000 to 160,000 and having the isoelectric point at pH 5.5 and toxicity 5.0--10.0 x 10(7) Dlm per 1 mg protein were obtained.

L15 ANSWER 18 OF 26 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 10
ACCESSION NUMBER: 1980:165880 BIOSIS
DOCUMENT NUMBER: BA69:40876
TITLE: THERMAL INACTIVATION OF CLOSTRIDIUM-**BOTULINUM TOXINS** TYPES A AND B IN **BUFFER** AND BEEF AND MUSHROOM PATTIES.
AUTHOR(S): BRADSHAW J G; PEELER J T; TWEDT R M
CORPORATE SOURCE: DIV. MICROBIOL., FOOD DRUG ADM., CINCINNATI, OHIO 45226, USA.
SOURCE: J FOOD SCI, (1979) 44 (6), 1653-1657.
CODEN: JFDSAZ. ISSN: 0022-1147.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB To determine the time-temperature relationships for the inactivation of botulinal toxins, crude toxins were prepared from 3 type A strains (62A, 73A, V141) and 2 type B strains (Beans-B and 999B). Toxins were diluted to 6700-32,000 mouse LD50 units/0.5 ml in beef and mushroom patties and in 0.1 M **phosphate buffer** at pH 6.05 and 0.1 M acetate **buffer**, pH 5.0, and were heated at temperatures from 67.8-80.0.degree. C. In the patties, inactivation times ranged from 53.15 min to 0.62 min and from 51.20

min to 1.08 min for the most thermostable type A (73A) and type B (Beans-B) toxins, respectively, whereas significantly less time was required in **phosphate buffer**.

L15 ANSWER 19 OF 26 TOXLIT
ACCESSION NUMBER: 1979:50569 TOXLIT
DOCUMENT NUMBER: CA-091-118322P
TITLE: Structure and toxicity of Clostridium botulinum type C Toxin.
AUTHOR: Syuto B; Kubo S
CORPORATE SOURCE: Fac. Vet. Med., Hokkaido Univ., Sapporo
SOURCE: Jpn. J. Med. Sci. Biol, (1979). Vol. 32, No. 2, pp. 132-3.
CODEN: JJMCAQ.
FILE SEGMENT: CA
LANGUAGE: English
OTHER SOURCE: CA 91:118322
ENTRY MONTH: 197910
AB C. **botulinum Toxin** C could be sepd. into 2 peptide chains by chromatog. of QAE-Sephadex A-50 with a linear gradient of NaCl in 6% 2-mercaptoethanol-borate **phosphate buffer** at pH 8.1 and 0.degree.. The components had different antigenicities and antitoxin to either chain neutralized the mother toxin toxicity. Combining the 2 chains gave an active form having 74% of the toxicity of the mother toxin; thus both chains are essential for toxicity. The reconstitution method affected the toxicity of the material prepd. from the chains. Tryptophan and tyrosine residues were crit. to maintain the toxin toxicity.

L15 ANSWER 20 OF 26 TOXLIT
ACCESSION NUMBER: 1979:33396 TOXLIT
DOCUMENT NUMBER: CA-091-001071Q
TITLE: Studies on the stability of purified and crude **botulinum toxin** of serotype B (strain ATCC 7949).
AUTHOR: Schwarz W
CORPORATE SOURCE: Inst. Lebensmittelkd., Fleischhyg. und -Technol., Tieraerztl. Hochsch. Hannover, Hannover
SOURCE: Arch. Lebensmittelhyg, (1979). Vol. 30, No. 1, pp. 29-33.
CODEN: ALMHAO.
FILE SEGMENT: CA
LANGUAGE: German
OTHER SOURCE: CA 91:1071
ENTRY MONTH: 197907
AB Crude and purified Clostridium **botulinum toxin** serotype B was stable for 2 wk in pH 4.5 0.05-0.1M **phosphate buffer**. Within the next 2 wk the toxicity decreased only

slightly.

L15 ANSWER 21 OF 26 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 11
ACCESSION NUMBER: 1978:195588 BIOSIS
DOCUMENT NUMBER: BA66:8085
TITLE: HEAT INACTIVATION OF **BOTULINUM TOXIN** TYPE A IN SOME CONVENIENCE FOODS AFTER FROZEN STORAGE.
AUTHOR(S): WOOLFORD A L; SCHANTZ E J; WOODBURN M J
CORPORATE SOURCE: FOOD RES. INST., UNIV. WIS., MADISON, WIS. 53706, USA.
SOURCE: J FOOD SCI, (1978) 43 (2), 622-624.
CODEN: JFDSAZ. ISSN: 0022-1147.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Crystalline type A toxin from the Hall Strain of Clostridium botulinum was added to beef pie fillings (ph 5.9), 0.05 M **phosphate buffer** (pH 5.9), cream of mushroom soup (pH 6.2) or tomato soup (pH 4.1) and 1 ml placed in 2-ml thin glass ampules. These were frozen and stored at -20.degree. C for 180 days. At timed intervals a few ampules were thawed and the contents tested for toxicity and for the rate of heat inactivation of the toxin. The toxicity of type A in the contents remained the same throughout the frozen storage. Although the literature reports show a decrease in the heat stability of type E toxin after frozen storage, the heat inactivation rates for type A remained the same. pH is 1 of the important variables affecting the heat stability of type A toxin dissolved in various **buffers**.

L15 ANSWER 22 OF 26 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 76202136 MEDLINE
DOCUMENT NUMBER: 76202136
TITLE: [Extraction and concentration of Clostridium **botulinum toxins** from specimens (author's transl)].
Extraktion und Anreicherung von Clostridium botulinum-Toxinen aus dem Untersuchungsmaterial.
AUTHOR: Sonnenschein B; Bisping W
SOURCE: ZENTRALBLATT FUR BAKTERIOLOGIE, PARASITENKUNDE, INFEKTIONSKRANKHEITEN UND HYGIENE. ERSTE ABTEILUNG ORIGINALE. REIHE A: MEDIZINISCHE MIKROBIOLOGIE UND PARASITOLOGIE, (1976 Mar) 234 (2) 247-59.
Journal code: Y52. ISSN: 0300-9688.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197609
AB In order to detect minimal amounts of Clostridium **botulinum**

toxins in animal tissue or food specimens it is necessary to use an extraction method which results in concentration of the botulinal toxins. In the present examinations, artificially contaminated canned beans were used to develop a suitable procedure for extraction and concentration of botulinal toxins A-E. The procedure consisted of 4 steps: 1. Canned beans were diluted 1:2 with 0.1 m **phosphate buffer** pH 6.0. 2. The diluted material was homogenised with an "Ultra-Turrax" homogeniser for 20 sec. 3. The monogenised material was centrifuged at 4000 rpm for 30 min. 4. 15 ml of supernatant was concentrated using a "Millipore ultrafiltration chamber" (with a membrane capable of excluding all material with a molecular weight above 25,000). A pressure of 1.5 atmospheres was applied until the terminal volume was 0.5 ml. Following extraction and concentration, the samples were assayed for botulinal toxin in mice. Using this assay the concentration of the five toxins were shown to be as follows: Type A toxin: 19.0-fold toxin concentration Type B toxin: 14.8-fold toxin concentration Type C toxin: 20.6-fold toxin concentration Type D toxin: 28.2-fold toxin concentration Type E toxin: 112.2-fold toxin concentration

L15 ANSWER 23 OF 26 MEDLINE
ACCESSION NUMBER: 72092593 MEDLINE
DOCUMENT NUMBER: 72092593
TITLE: Heat resistance of spores of marine and terrestrial strains of Clostridium botulinum type C.
AUTHOR: Segner W P; Schmidt C F
SOURCE: APPLIED MICROBIOLOGY, (1971 Dec) 22 (6) 1030-3.
Journal code: 6K0. ISSN: 0003-6919.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197205

L15 ANSWER 24 OF 26 MEDLINE
ACCESSION NUMBER: 70107475 MEDLINE
DOCUMENT NUMBER: 70107475
TITLE: A study of the effect of ionizing radiation on resistance, germination, and toxin synthesis of Clostridium botulinum spores, types A, B, and E. COO-1095-3.
AUTHOR: Graikoski J T; Kempe L L
SOURCE: COO REPORTS, (1966 Jan 14) 1-100.
Journal code: COZ.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
ENTRY MONTH: 197005

L15 ANSWER 25 OF 26 TOXLINE
ACCESSION NUMBER: 1970:8942 TOXLINE
DOCUMENT NUMBER: TOXBIB-70-107475
TITLE: A study of the effect of ionizing radiation on resistance, germination, and toxin synthesis of Clostridium botulinum spores, types A, B, and E. COO-1095-3.
AUTHOR: Graikoski J T; Kempe L L
SOURCE: COO REPORTS, (1966). COO Rep, 1966, P1-100. Journal code: COZ.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: TOXBIB
LANGUAGE: English
OTHER SOURCE: MEDLINE 70107475
ENTRY MONTH: 197005

L15 ANSWER 26 OF 26 TOXLINE
ACCESSION NUMBER: 1981:23412 TOXLINE
DOCUMENT NUMBER: NTIS-AD-258-991-9
TITLE: Phagocytosis of Staphylococci by Mouse Leukocytes in the Presence of **Botulinum Toxin**.
AUTHOR: FREEMAN N L
CORPORATE SOURCE: California Univ Oakland Naval Biological Lab.
CONTRACT NUMBER: Contract nonr22273
SOURCE: Govt Reports Announcements & Index (GRA&I), (1960). No. 24. NTIS Price: MF A01. NTIS Order No.: NTIS/AD-258 991/9, Distribution limitation now removed. NOTE: Only 35mm microfilm is available. No microfiche., 10p
FILE SEGMENT: NTIS
LANGUAGE: Unavailable
ENTRY MONTH: 198105
AB TD3: The moderately high concentration of crystalline type A **botulinum toxin** used in this study did not significantly decrease the phagocytic activity of mouse leukocytes, in that the indices obtained with active toxin were comparable to the indices obtained with thermally inactivated toxin or gelatin-**phosphate buffer**. Similar results were obtained with rabbit leukocytes. Phagocyto i appeared to be enhanced in the saline controls; rotating the leukocyte preparations for 60 min at 37 C depressed phagocytic activity. The results of individual experiments varied considerably, but cumulative results were not statistically significant. (Author)

(FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, TOXLIT, TOXLINE, PHIC, PHIN' ENTERED AT 14:25:14 ON 26 SEP 2000)
L16 267 S MOYER E?/AU
L17 35 S HIRTZER P?/AU
- Author(s)

Searcher : Shears 308-4994

L18 3 S L16 AND L17
L19 299 S L16 OR L17
L20 5 S L19 AND L6
L21 5 S L18 OR L20
L22 4 DUP REM L21 (1 DUPLICATE REMOVED)

L22 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 1
ACCESSION NUMBER: 2000:190943 CAPLUS
DOCUMENT NUMBER: 132:227422
TITLE: Stable liquid formulations of **Botulinum toxin**
INVENTOR(S): **Moyer, Elizabeth; Hirtzer, Pamela**
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000015245	A2	20000323	WO 1999-US20912	19990909
WO 2000015245	A3	20000608		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9958214	A1	20000403	AU 1999-58214	19990909
PRIORITY APPLN. INFO.:			US 1998-99870	19980911
			WO 1999-US20912	19990909

AB The invention includes liq. formulations of **botulinum toxin** that are stable to storage in liq. form at std. refrigerator temps. for at least 1-2 yr and to storage at higher temps. for at least 6 mo. The invention also includes methods of treatment using such formulations and uses of such formulations in the manuf. of medicaments for various therapeutic and cosmetic treatments. A formulation was prepd. contg. **Botulinum toxin** Type B 500.+-.100 LD50U/mL, di-Na succinate 10 mM, NaCl 100 mM, human albumin 0.5 mg/mL, and HCl for pH adjustment.

L22 ANSWER 2 OF 4 TOXLIT
ACCESSION NUMBER: 2000:11654 TOXLIT
DOCUMENT NUMBER: CA-132-227422G
TITLE: Stable liquid formulations of **Botulinum**

toxin.

AUTHOR: **Moyer E; Hirtzer P**
SOURCE: (2000). PCT Int. Appl. PATENT NO. 0015245 03/23/2000 (Elan Pharmaceuticals, Inc.).
CODEN: PIXXD2.
PUB. COUNTRY: UNITED STATES
DOCUMENT TYPE: Patent
FILE SEGMENT: CA
LANGUAGE: English
OTHER SOURCE: CA 132:227422
ENTRY MONTH: 200004

AB The invention includes liq. formulations of **botulinum toxin** that are stable to storage in liq. form at std. refrigerator temps. for at least 1-2 yr and to storage at higher temps. for at least 6 mo. The invention also includes methods of treatment using such formulations and uses of such formulations in the manuf. of medicaments for various therapeutic and cosmetic treatments. A formulation was prepd. contg. **Botulinum toxin** Type B 500.+-.100 LD50U/mL, di-Na succinate 10 mM, NaCl 100 mM, human albumin 0.5 mg/mL, and HCl for pH adjustment.

L22 ANSWER 3 OF 4 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1994:189289 BIOSIS
DOCUMENT NUMBER: PREV199497202289
TITLE: **Botulinum toxin** type B: Experimental and clinical experience.
AUTHOR(S): **Moyer, Elizabeth**; Setler, Paulette E.
CORPORATE SOURCE: Athena Neurosciences Inc., South San Francisco, CA USA
SOURCE: Jankovic, J. [Editor]; Hallett, M. [Editor]. Neurological Disease and Therapy, (1994) Vol. 25, pp. 71-85. Neurological Disease and Therapy; Therapy with botulinum toxin.
Publisher: Marcel Dekker, Inc. 270 Madison Avenue, New York, New York 10016, USA.
ISSN: 1058-7535. ISBN: 0-8247-8824-9.
DOCUMENT TYPE: Book
LANGUAGE: English

L22 ANSWER 4 OF 4 TOXLINE
ACCESSION NUMBER: 1994:47428 TOXLINE
DOCUMENT NUMBER: BIOSIS-94-14143
TITLE: **BOTULINUM TOXIN** TYPE B EXPERIMENTAL AND CLINICAL EXPERIENCE.
AUTHOR: **MOYER E**; SETLER P E
SOURCE: (1994). pp. 71-85. JANKOVIC, J. AND M. HALLETT (ED.). NEUROLOGICAL DISEASE AND THERAPY, VOL. 25. THERAPY WITH BOTULINUM TOXIN. XXVI+608P. MARCEL DEKKER, INC.: NEW YORK, NEW YORK, USA; BASEL, SWITZERLAND. ISBN

0-8247-8824-9.
CODEN: NDTHEE.
FILE SEGMENT: BIOSIS
LANGUAGE: English
ENTRY MONTH: 199406
AB BIOSIS COPYRIGHT: BIOL ABS. RRM BOOK CHAPTER CLOSTRIDIUM-BOTULINUM MOUSE GUINEA-PIG RABBIT **BOTULINUM TOXIN** AUTONOMIC-DRUG TOXIN STRUCTURE TOXIN-NONTOXIC PROTEIN COMPLEX PHARMACOLOGY TOXICOLOGY COMPARATIVE MUSCLE PARALYTIC EFFICACY COMPARATIVE TOXICITY DATA CLINICAL USE PHARMACODYNAMICS

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Devi, S.
09/393590

09/393590

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*File 35: File has resumed updating, see HELP NEWS 35.
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(c) 2000 Cambridge Sci Abs
File 144:Pascal 1973-2000/Sep W4
(c) 2000 INIST/CNRS
*File 144: This file is updating weekly now.
File 266:FEDRIP 2000/Aug
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File 440:Current Contents Search(R) 1990-2000/Oct W1
(c) 2000 Inst for Sci Info
File 348:European Patents 1978-2000/Sep W04
(c) 2000 European Patent Office
File 357:Derwent Biotechnology Abs 1982-2000/Oct B1
(c) 2000 Derwent Publ Ltd
File 113:European R&D Database 1997
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Set	Items	Description

? ds; t 6/3,ab/1-27

Set	Items	Description
S1	4347	BOTULINUM(W)TOXIN? ? OR BT(10N)BOTULINUM
S2	46	S1 AND BUFFER?
S3	23	S2 AND (PHOSPHATE OR CITRATE OR SUCCINATE)
S4	24	S2 AND (FORMUL? OR COMPOSITION? ? OR COMP???)
S5	30	S3 OR S4
S6	27	RD (unique items)

- key terms

>>>No matching display code(s) found in file(s): 65, 113

6/3,AB/1 (Item 1 from file: 35)
DIALOG(R)File 35:Dissertation Abstracts Online
(c) 2000 UMI. All rts. reserv.

01637297 AAD9827004
A BIOPHYSICAL CHARACTERIZATION OF *BOTULINUM"** *TOXIN"** AND CHOLERA TOXIN (RECEPTOR, BIO SENSOR FILM, KILODALTON *COMPLEX"**)
Author: KUZIEMKO, GEOFFREY MATTHEW
Degree: PH.D.
Year: 1997
Corporate Source/Institution: UNIVERSITY OF CALIFORNIA, BERKELEY (0028)
Source: VOLUME 59/03-B OF DISSERTATION ABSTRACTS INTERNATIONAL.
Searcher : Shears 308-4994

PAGE 1097. 149 PAGES

This thesis describes the biophysical characterization of two microbial toxins--*botulinum"** *toxin"** and cholera toxin--(md applications of this characterization to the development of new bio-sensors for these deadly pathogens.

Electron microscopy was used to acquire a two-dimensional image map of the 900 kDa *botulinum"** *toxin"** *complex"**. Based upon the image map, and the hydrodynamic radius, a model for the three-dimensional structure of the *complex"** is presented. The stability of the *complex"**, the toxin, and the non-toxic proteins was examined using circular dichroism and dynamic light scattering under a variety of *buffers"** ranging from pH 2-10. Results indicated that, when uncomplexed, the toxin and non-toxic proteins are least stable at acidic pH; however, when complexed, the proteins are most stable at acidic pH. The stability was further studied by performing protease incubations with pepsin, trypsin, chymotrypsin and carboxypeptidase. Uncomplexed *botulinum"** *toxin"** and the uncomplexed non-toxic proteins were completely proteolyzed. Yet, when in the complexed form, the *botulinum"** *toxin"** survived the protease incubations. Based on these experiments, a molecular rationale for the delivery of *botulinum"** *toxin"**, through the gastrointestinal tract, is proposed. To further the understanding of the relationship between the toxin and the *complex"**, the structural relationship between the 150 kilodalton toxin and the 900 kilodalton *complex"** was investigated by antibody mapping. The mapping used 44 single-chain variable fragments that recognized the individual domains of the toxin. Surprisingly, the results of the mapping indicated that the binding domain, in comparison to the catalytic domain, was covered by the *complex"**. These findings are critical for the development of *botulinum"** *toxin"** vaccines, which target the binding domain.

To further the understanding of toxin-receptor recognition, the cholera toxin-ganglioside system was investigated. The binding series for the ganglioside family was correlated with the structure of the cholera toxin binding domain to determine the most important oligosaccharide residues involved in the cholera toxin-receptor interaction. Finally, the knowledge of bacterial toxin-receptor interactions was combined with recent advances in the field of material science to develop a new type of bio-sensor film that detects the binding of toxins to synthetic membranes and induces a colorimetric response.

6/3,AB/2 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal

13191309 PASCAL No.: 97-0455265
Identification of a recombinant synaptobrevin-thioredoxin fusion protein by capillary zone electrophoresis using laser-induced fluorescence detection

ASERMELY K E; BROOMFIELD C A; NOWAKOWSKI J; COURTNEY B C; ADLER M
ISSAQ H J, ed
Neurotoxicology Branch, Pharmacology Division, U.S. Army Medical Research Institute of Chemical Defense, 3100 Ricketts Point Road, Aberdeen Proving Ground, MD 21010-5425, United States; Biochemical Pharmacology Branch, Pharmacology Division, U.S. Army Medical Research Institute of Chemical Defense, 3100 Ricketts Point Road, Aberdeen Proving Ground, MD 21010-5425, United States; Applied Pharmacology Branch, Pharmacology Division, U.S. Army Medical Research Institute of Chemical Defense, 3100 Ricketts Point Road, Aberdeen Proving Ground, MD 21010-5425, United States
Annual Frederick Conference on Capillary Electrophoresis, 7 (Frederick, MD USA) 1996-10-21
Journal: Journal of chromatography. B. Biomedical sciences and applications, 1997, 695 (1) 67-75
Language: English
Capillary zone electrophoresis (CZE) was utilized to identify a synaptobrevin-thioredoxin fusion protein (TSB-51). TSB-51 is a substrate for cleavage by *botulinum"** *toxin"** B at the Q(76)-F(77) site. TSB-51 was derivatized with a fluorophore, CBQCA (3-(4-carboxy-benzoyl)-2-quinolin e-carboxaldehyde), for 4 h at room temperature. Optimal conditions for CZE separation of the TSB-51-CBQCA *complex"** were determined: *buffer"** (sodium borate), pH (9.0), applied voltage (25 kV), temperature (25 Degree C) and forward polarity. SDS-PAGE showed that TSB-51 had a molecular mass of similar 19 kDa. The protein was transferred to PVDF membrane and sequenced by the Edman degradation method verifying the first twelve amino acids as SDKIIHLTDDSF. TSB-51 was also collected during CZE separation and subsequently sequenced yielding the first three amino acids as SDK. This CZE-LIF method coupled with the CBQCA derivatization, fraction collection and Edman sequencing allowed for identification of the recombinant protein, a fast separation run time and utilization of small volumes of peptide (1.5 ng protein/23.6 nl injection). This method will be used for monitoring the endopeptidase activity of *botulinum"** *toxin"** B on TSB-51.

6/3,AB/3 (Item 2 from file: 144)
DIALOG(R)File 144:Pascal

12119947 PASCAL No.: 95-0350497
Adsorption of *botulinum"** *toxin"** to activated charcoal with a mouse bioassay
GOMEZ H F; JOHNSON R; GUVEN H; MCKINNEY P; PHILLIPS S; JUDSON F; BRENT J
Univ. Colorado health sci. cent., Denver health hosp., Rocky Mountain poison drug cent., USA
American Academy of Clinical Toxicology annual scientific meeting (Tampa FL USA) 1992-09
Journal: Annals of emergency medicine, 1995, 25 (6) 818-822

Language: English
Study objective: We evaluated the effectiveness of activated charcoal (AC) in adsorbing Clostridium botulinum type A toxin using a mouse bioassay. Design: Prospective, blinded, randomized, controlled animal study. Setting: Animal care facility. Participants: One hundred forty Swiss/Webster ND-4 strain mice. Intervention: Food contaminated with type A *botulinum"** *toxin"** was homogenized in a *phosphate"**/gel *buffer"** (pH 6.2). The concentrate was diluted by factors of 1:10, 1:50, and 1:100. AC was added to aliquots of the dilutions to a 20% final concentration. The samples were centrifuged, supernatant was removed, and separate groups of mice were injected intraperitoneally with.5 mL of each dilution (those treated with AC and controls untreated with AC). The animals were then observed over 5 days for signs of botulism. Results: None of the 60 animals injected intraperitoneally with dilutions treated with AC was observed to have any signs of botulism. In contrast, deaths were observed in 10 of 20, 9 of 20 and 4 of 20 mice injected with untreated dilutions of 1:100, 1:50, and 1:10, respectively (P<.004). Conclusion: In this model, treatment of *botulinum"** *toxin"** with AC before administration resulted in greatly reduced morbidity and mortality

6/3,AB/4 (Item 1 from file: 266)
DIALOG(R)File 266:FEDRIP

00305729
IDENTIFYING NO.: 5P01GM51487-07 0006 AGENCY CODE: CRISP
MOLECULAR STRUCTURE OF THE 900 KD BOTULINUM NEUROTOXIN *COMPLEX"**
PRINCIPAL INVESTIGATOR: STEVENS, RAYMOND
ADDRESS: EO LAWRENCE BERKELEY NATL LAB 1 CYCLOTRON ROAD BERKELEY, CA 94720
PERFORMING ORG.: UNIVERSITY OF CALIF-LAWRENC BERKELEY LAB, BERKELEY, CALIFORNIA
SPONSORING ORG.: NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES
FY : 2000
SUMMARY: Botulinum neurotoxin *complex"** serotype A is a 900 kiloDalton (kDa) protein produced as one of eight serotypes (A-G) by the anaerobic bacterium Clostridium botulinum. Among the most potent biological toxins known to man, botulinum neurotoxin causes inhibition of synaptic vesicle release at the neuromuscular junction resulting in flaccid paralysis and ultimately death. Botulinum neurotoxin type A (BoNT/A) is a potent disease agent in both food-borne botulism and Sudden Infant Death Syndrome (SIDS), an established biological weapon, and a novel therapeutic in the treatment of involuntary muscle disorders. Previously, we have determined the 3-D structure of the 150 kDNA neurotoxin component of the 900 kDa *complex"** by x-ray crystallography. We have also completed antibody mapping experiments to determine how the 150 kDa neurotoxin is bound into the 900 kDa toxin *complex"**. We have conducted a series of biophysical stability experiments in order to understand how the two assemblies (150 kDa toxin

and 750 kDa non-toxic component) combine and stabilize the 900 kDa *complex"** . Lastly, based on the work above, and preliminary electron microscopy work, we are designing an alternative vaccine strategy for botulism. Current vaccine programs for botulism are not very effective.

The preliminary objective of this proposal is to obtain a three-dimensional structure of the 900 kDa botulinum neurotoxin *complex"**, and understand how the neurotoxin component fits into the *complex"**. To accomplish this goal, we will use a 2-D crystals of the 900 kDa *complex"** to conduct 3-D image reconstruction experiments. We have already obtained 2-D crystals of the 900 kDa *complex"** to conduct 3-D image reconstruction experiments. We have already obtained 2-D crystals of the 900 kDa *complex"** that diffract weakly to 14 Angstroms resolution in negative strain, and a density projection map has been produced at 30 Angstroms resolution. Based on the crystal quality and the frequency with which defects were observed in the crystals used in our earlier investigation, it appears as though much higher quality crystals can be obtained. Specifically, our transfer technique is presently crude due to our new venture into this area of research, and several suggestions have been made by other program project members on how to improve our transfer techniques. We are also investigating alternative *buffer"** conditions to help stabilize the protein further. Once optimization of the 2-D crystals has been completed, we will complete the negative stain work at the maximum resolution possible using data collection in a tilt series followed by 3-D image reconstruction. This work will be followed by attempting higher resolution studies with cryo-techniques. We will crystallize the 900 kDa *complex"** in the presence of scFv antibody molecules that have a high affinity for exposed regions of the neurotoxin when bound to the 900 kDn *complex"**.

6/3,AB/5 (Item 1 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

10652984 GENUINE ARTICLE#: 206FD NUMBER OF REFERENCES: 12
TITLE: Detection of sparse *botulinum"** *toxin"** A binding sites using fluorescent latex microspheres
AUTHOR(S): Crosland RD (REPRINT); Canziani GA
CORPORATE SOURCE: USA, Toxinol Div, /Frederick//MD/21702 (REPRINT); USA, Toxinol Div, /Frederick//MD/21702
PUBLICATION TYPE: JOURNAL
PUBLICATION: JOURNAL OF HISTOTECHNOLOGY, 1999, V22, N2 (JUN), P113-115
PUBLISHER: NATL SOC HISTOTECHNOLOGY, 4201 NORTHVIEW DR, STE 502, BOWIE, MD 20716-1073 USA
ISSN: 0147-8885
LANGUAGE: English DOCUMENT TYPE: ARTICLE
ABSTRACT: The most potent toxins known are produced by strains of Clostridium botulinum. To paralyze the vertebrate neuromuscular junction, the toxins bind selectively to nerve endings, translocate

into the presynaptic terminal, and hydrolyze proteins of the exocytotic apparatus, thus inhibiting the release of acetylcholine. Our goal was to develop a convenient, reliable technique to detect specific binding of *botulinum"** *toxin"** A to its targets, a technique that could be easily modified to detect the binding sites of other ligands as well. Our method utilized fluorescent latex microspheres and is theoretically capable of detecting a single binding site at the light microscopic level.

Nonspecific binding sites on 7-mu m thick sections of unfixed, cryosectioned mouse diaphragm were first blocked with 20% goat serum in *phosphate"**-*buffered"** saline (GSI PBS). We incubated the diaphragm for 1 hr at 22 degrees with various concentrations of *botulinum"** *toxin"** A in GS/PBS, followed by incubation with rabbit anti-*botulinum"** *toxin"** A antiserum, biotin-labeled,goat anti-rabbit antibody, and finally avidin-labeled, 0.03 mu m diameter, fluorescent latex microspheres.

As expected, binding was localized to the area of the neuromuscular junction. Binding was also observed in association with axons innervating some junctions. We could detect binding on diaphragms that were exposed to as little as 10 pM *botulinum"** *toxin"** A, which is in the low range of effective in vitro doses that block neuromuscular transmission. This is a convenient, sensitive, and specific technique for detecting *botulinum"** *toxin"** A binding sites that is easily modifiable for the detection of binding sites of other ligands as well.
ISSN: 0147-8885

6/3,AB/6 (Item 2 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

09281509 GENUINE ARTICLE#: ZB344 NUMBER OF REFERENCES: 18
TITLE: A comparison of the spread of three *formulations"** of botulinum neurotoxin A as determined by effects on muscle function
AUTHOR(S): Dodd SL (REPRINT); Rowell BA; Vrabas IS; Arrowsmith RJ; Weatherill PJ
CORPORATE SOURCE: UNIV FLORIDA,COLL HLTH & HUMAN PERFORMANCE, 27 FLG/GAINESVILLE//FL/32611 (REPRINT); SPEYWOOD PHARMACEUT LTD,/MAIDENHEAD SL6 4UH/BERKS/ENGLAND/
PUBLICATION TYPE: JOURNAL
PUBLICATION: EUROPEAN JOURNAL OF NEUROLOGY, 1998, V5, N2, P181-186
PUBLISHER: RAPID SCIENCE PUBLISHERS, 2-6 BOUNDARY ROW, LONDON, ENGLAND SE1 8NH
ISSN: 1351-5101
LANGUAGE: English DOCUMENT TYPE: ARTICLE
ABSTRACT: The purpose of these experiments was to *compare"** the spread of three *formulations"** of botulinum neurotoxin A. A gelatin/

*phosphate"** *buffer"** (C), Dysport(R) (D {0.5 U}, Botox(R) (B {0.167 U}), or a purified preparation of botulinum neurotoxin A [Bont A] (BA {0.5 U}) was injected into the tibialis anterior of male, Wistar rats. After 4 days, the adjacent extensor digitorum longus muscle was isolated in situ and the nerve was maximally stimulated to determine contractile properties and the rate of fatigue. There were no differences in body or muscle weights between any of the groups after 4 days of treatment. Maximal twitch and tetanic tensions were decreased approximate to 25% ($p < 0.05$) in all treatment groups compared to C. In addition, rate of tension development was significantly less in all treatment groups compared to C but one-half relaxation time and time to peak tension were not different between any groups. Fatigue of the muscle was significantly faster in all groups compared to C but there was no difference between treatment groups. These data indicated that *botulinum"** *toxin"** A injected intramuscularly was likely to spread to adjacent muscles but that the spread was not different between the three *formulations"** tested. The effect of the spread ranged from a slight to a severe reduction in maximal tension but this did not occur in all animals studied. (C) 1998 Rapid Science Ltd.

ISSN: 1351-5101

6/3,AB/7 (Item 1 from file: 348)

01148808

Carrier for immobilizing biologically active substance

Trager zur Immobilisierung von biologisch aktiven Substanzen

Support pour l'immobilisation de substances biologiquement actives

PATENT ASSIGNEE:
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Matsumura, Yoshiyuki, c/o Nisshinbo Industries Co., Tokyo Res. Ctr., 18-1 NishiArai Sakae-cho 1-chome, Adachi-ku, Tokyo, (JP)

LEGAL REPRESENTATIVE:
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PATENT (CC, No, Kind, Date): EP 1001267 A2 000517 (Basic)
EP 1001267 A3 000906
APPLICATION (CC, No, Date): EP 99308958 991110;
PRIORITY (CC, No, Date): JP 98318924 981110; JP 98318925 981110
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE

EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: G01N-033/545; C12Q-001/68

ABSTRACT EP 1001267 A2
A base material having an isocyanate group or a carbodiimide group on its surface is used as a carrier for immobilizing a biologically active substance to analyze a first biologically active substance or a second biologically active substance in a sample, wherein the first substance immobilized on the carrier is reacted with the second substance capable of specifically binding to the first substance, and the second substance indirectly bound to the carrier by the bond between it and the first substance or the second substance that is bound to the carrier is detected.
ABSTRACT WORD COUNT: 94

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200020	594
SPEC A	(English)	200020	10027
Total word count - document A			10621
Total word count - document B			0
Total word count - documents A + B			10621

6/3,AB/8 (Item 2 from file: 348)
DIALOG(R)File 348:European Patents

01126154
Stabilization of cooked meat *compositions"** using whey from nisin-producing cultures
Stabilisierung von gekochten Fleischzusammensetzungen mit Molke von Nisin produzierenden Kulturen
Stabilisation des *compositions"** contenant de la viande cuite en utilisant du petit-lait de cultures produisant de la nisine
PATENT ASSIGNEE:
KRAFT FOODS, INC., (1186184), Three Lakes Drive, Northfield, Illinois 60093, (US), (Applicant designated States: all)
INVENTOR:
Nauth, Kaiser Rajinder, 455 Anita Place, Wheeling, Illinois 60090, (US)
Ruffie, Debora Diane, 1435 East Emmerson Lane, Mount Prospect, Illinois 60056, (US)
Roman, Michael Gerard, 112 Windjammer Lane, Grayslake, Illinois 60030, (US)
LEGAL REPRESENTATIVE:
Eyles, Christopher Thomas (30482), W.P. THOMPSON & CO. Celcon House 289-293 High Holborn, London WC1V 7HU, (GB)
PATENT (CC, No, Kind, Date): EP 983724 A1 000308 (Basic)
Searcher : Shears 308-4994

APPLICATION (CC, No, Date): EP 99306902 990831;
PRIORITY (CC, No, Date): US 98465 980831
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: A23B-004/20

ABSTRACT EP 983724 A1

The present invention provides a stabilized meat product of cooked meat comprising cooked meat and nisin-containing whey. The nisin-containing whey is prepared by a inoculating a pasteurized dairy *composition"** with a culture of a nisin-producing microorganism, incubating the *composition"** until the pH attains a value between about 6.2 and about 2.0 and a whey and curd mixture is formed, and separating the whey from the whey and curd mixture to give the separated whey which is the nisin-containing whey. The invention also provides a method of making a stabilized meat product of cooked meat, that includes preparing a *composition"** including meat and nisin-containing whey, and cooking the *composition"**. The invention additionally provides a method of inhibiting the growth of a pathogenic microorganism in cooked meat that includes preparing a *composition"** comprising meat and nisin-containing whey, sealing the cooked *composition"** into packaging, and cooking the *composition"**; whereby the growth of a pathogenic microorganism is inhibited.

ABSTRACT WORD COUNT: 155
NOTE:
Figure number on first page: 1

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200010	793
SPEC A	(English)	200010	5147
Total word count - document A			5940
Total word count - document B			0
Total word count - documents A + B			5940

6/3,AB/9 (Item 3 from file: 348)
DIALOG(R)File 348:European Patents

00941408
PROCESSES FOR PRODUCING SUGAR NUCLEOTIDES AND *COMPLEX"** CARBOHYDRATES
PROZESSE FUR DIE PRODUKTION VON ZUCKER-NUKLEOTIDEN UND KOMPLEXEN KOHLEHYDRATEN
PROCEDES DE PRODUCTION DE NUCLEOTIDES DE SUCRE ET DE GLUCIDES COMPLEXES
PATENT ASSIGNEE:
KYOWA HAKKO KOGYO CO., LTD., (229061), Ohtemachi Bldg., 6-1, Ohtemachi

1-chome, Chiyoda-ku, Tokyo 100, (JP), (applicant designated states: AT;BE;CH;DE;DK;ES;FI;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)

INVENTOR:
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TABATA, Kazuhiko, 4-17-9, Morino, Machida-shi Tokyo 194, (JP)
OZAKI, Akio, 3-9-13, Naka-machi, Machida-shi Tokyo 194, (JP)
LEGAL REPRESENTATIVE:
VOSSIUS & PARTNER (100311), Postfach 86 07 67, 81634 Munchen, (DE)

PATENT (CC, No, Kind, Date): EP 870841 A1 981014 (Basic)
WO 9812343 980326
APPLICATION (CC, No, Date): EP 97940365 970912; WO 97JP3226 970912
PRIORITY (CC, No, Date): JP 96244451 960917; JP 96285066 961028
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: C12P-019/26; C12N-001/21; C12N-015/54; C12N-005/16; C12P-019/26; C12R-001/19; C12R-001/15

ABSTRACT EP 870841 A1

This invention relates to a process for producing a sugar nucleotide, in which a) a culture broth of a microorganism capable of producing NTP from a nucleotide precursor, or a treated product of the culture broth, and b) a culture broth of a microorganism capable of producing a sugar nucleotide from a sugar and NTP, or a treated product of the culture broth, are used as enzyme sources; a process for producing a *complex"** carbohydrate, in which the above-described a) and b) and c) a culture broth of a microorganism, an animal cell or an insect cell capable of producing a *complex"** carbohydrate from a sugar nucleotide and a *complex"** carbohydrate precursor, or a treated product of the culture broth, are used as enzyme sources; a process for producing a *complex"** carbohydrate, in which a culture broth of a microorganism, an animal cell or an insect cell capable of producing a *complex"** carbohydrate from a sugar nucleotide and a *complex"** carbohydrate precursor, or a treated product of the culture broth, is as an enzyme source; and a process for producing N-acetylglucosamine-1-*phosphate"**, in which a culture broth of a microorganism having strong galactokinase activity, or a treated product of the culture broth, is used as the enzyme source.
ABSTRACT WORD COUNT: 208

LANGUAGE (Publication,Procedural,Application): English; English; Japanese
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	9842	2773
SPEC A	(English)	9842	21085
Total word count - document A			23858
Total word count - document B			0
Total word count - documents A + B			23858

6/3,AB/10 (Item 4 from file: 348)
DIALOG(R)File 348:European Patents

00933023
MEDICINES COMPRISING Rho KINASE INHIBITOR
MEDIKAMENTE ENTHALTEND Rho-KINASE INHIBITOREN
MEDICAMENTS COMPRENANT UN INHIBITEUR DE LA Rho KINASE
PATENT ASSIGNEE:
YOSHITOMI PHARMACEUTICAL INDUSTRIES, LTD., (208562), 6-9, Hiranomachi 2-chome Chuo-ku, Osaka-shi Osaka 541, (JP), (Applicant designated States: all)
INVENTOR:
UEHATA, Masayoshi, Yoshitomi Phar. Ind. Ltd., Res. Lab., 7-25, Koyata 3-chome, Iruma-shi, Saitama 358, (JP)
ONO, Takashi, Yoshitomi Pharm. Ind., Ltd, Res. Lab., 7-25, Koyata 3-chome , Iruma-shi, Saitam 358, (JP)
SATOH, Hiroyuki, Yoshitomi Phar. Ind. Ltd., Res. Lab., 955, Oaza-Koiwai, Yoshitomimachi, Chikujo-gun, Fukuoka 871, (JP)
YAMAGAMI, Keiji, Yoshitomi Phar. Ind. Ltd., Res. Lab., 7-25, Koyata 3-chome, Iruma-shi, Saitama 358, (JP)
KAWAHARA, Toshio, Yoshitomi Phar. Ind. Ltd., Res. Lab., 955, Oaza-Koiwai, Yoshitomimachi, Chikujo-gun, Fukuoka 871, (JP)
LEGAL REPRESENTATIVE:
Weber, Thomas, Dr.Dipl.-Chem. et al (75092), Patentanwalte von Kreisler-Selting-Werner, Postfach 10 22 41, 50462 Koln, (DE)
PATENT (CC, No, Kind, Date): EP 956865 A1 991117 (Basic)
WO 9806433 980219
APPLICATION (CC, No, Date): EP 97934756 970808; WO 97JP2793 970808
PRIORITY (CC, No, Date): JP 96212409 960812
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; RO; SI
INTERNATIONAL PATENT CLASS: A61K-045/00; A61K-031/16; A61K-031/165; A61K-031/195; A61K-049/00; A61K-031/445; A61K-031/50; A61K-031/495; A61K-031/44; C07D-213/81; C07D-401/12

ABSTRACT EP 956865 A1
A Rho kinase inhibitor is provided as a novel pharmaceutical agent, particularly as a therapeutic agent of hypertension, a therapeutic agent of angina pectoris, a suppressive agent of cerebrovascular contraction, a therapeutic agent of asthma, a therapeutic agent of peripheral circulation disorder, a prophylactic agent of immature birth, a therapeutic agent of arteriosclerosis, an anti-cancer drug, an anti-inflammatory agent, an immunosuppressant, a therapeutic agent of autoimmune disease, an anti-AIDS drug, a contraceptive, a prophylactic agent of digestive tract infection, a therapeutic agent of osteoporosis, a therapeutic agent of retinopathy and a brain function improving drug.

In addition, the Rho kinase inhibitor is provided as a reagent and a diagnostic.
ABSTRACT WORD COUNT: 110

LANGUAGE (Publication,Procedural,Application): English; English; Japanese
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	9946	1777
SPEC A	(English)	9946	13010
Total word count - document A			14787
Total word count - document B			0
Total word count - documents A + B			14787

6/3,AB/11 (Item 5 from file: 348)
DIALOG(R)File 348:European Patents

00927121
Neurotoxin for cutaneous disorders in mammals
Neurotoxine zur Behandlung von Hauterkrankungen bei Saugetieren
Neurotoxines pour le traitement d'affections cutanees chez les mammiferes
PATENT ASSIGNEE:
Binder, William J., (1192732), 1640 Amalfi Drive, Pacific Palisades, California, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FI;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
INVENTOR:
Binder, William J., 1640 Amalfi Drive, Pacific Palisades, California, (US)
LEGAL REPRESENTATIVE:
Patentanwalte Schaad, Balass, Menzl & Partner AG (100781), Dufourstrasse 101 Postfach, 8034 Zurich, (CH)
PATENT (CC, No, Kind, Date): EP 845267 A1 980603 (Basic)
APPLICATION (CC, No, Date): EP 96118958 961127;
PRIORITY (CC, No, Date): EP 96118958 961127
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61K-038/16
ABSTRACT EP 845267 A1
A neurotoxin is used for the manufacture of a medicament for treatment of cutaneous cell-proliferative disorders in mammals. More specifically, the invention is useful in mitigating and inducing remission of lesions associated with such disorders and in controlling related symptoms of the disorders (such as scaling and itching). The medicament containing the invertebrate neurotoxin is administered to the skin of the host at or near the site of a lesion. The preferred neurotoxin for use in the invention is *Botulinum"** *toxin"**, particularly *Botulinum"** *toxin"** A.
ABSTRACT WORD COUNT: 86

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	9823	170
SPEC A	(English)	9823	3155
Total word count - document A			3325
Total word count - document B			0
Total word count - documents A + B			3325

6/3,AB/12 (Item 6 from file: 348)
DIALOG(R)File 348:European Patents

00910585
Polyetheresters copolymers as drug delivery matrices
Polyetherester-Copolymere als Matrixmaterialien fur die Arzneistoffabgabe
Copolymeres de polyetheresters comme matrice pour la delivrance de medicaments
PATENT ASSIGNEE:
Osteotech, Inc.,, (1118232), 51 James Way, Eatontown, NJ 07724, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FI;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
INVENTOR:
Goedemoed, Jacob Hillebrand, Frans van Mierisstraat 129-2, 1071 RR Amsterdam, (NL)
Hennink, Wilhelmus Everhardus, Zuidplaslaan 120, 2743 CZ Waddinxveen, (NL)
Bezemer, Jeroen Mattijs, Pieter Breughelstraat 97, 7556 ZK Hengelo, (NL)
Feijen, Jan, Oude Grensweg 96, 7552 GD Hengelo, (NL)
Van Blitterswijk, Clemens Antoni, Hekendorpsebuurt 2, 3467 PD Hekendorp, (NL)
De Bruijn, Joost Dick, Laan van Meerdervoort 67, 2517 AG Den Haag, (NL)
LEGAL REPRESENTATIVE:
de Bruijn, Leendert C. et al (19641), Nederlandsch Octrooibureau P.O. Box 29720, 2502 LS Den Haag, (NL)
PATENT (CC, No, Kind, Date): EP 830859 A2 980325 (Basic)
EP 830859 A3 980722
APPLICATION (CC, No, Date): EP 97202533 970818;
PRIORITY (CC, No, Date): US 699896 960816
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61K-009/16

ABSTRACT EP 830859 A2
A *composition"** for delivering a biologically active agent to a host. The *composition"** comprises a product including a biologically active agent encapsulated in a matrix comprising a copolymer, of a polyalkylene

glycol and an aromatic polyester, such as a polyethylene glycol terephthalate/polybutylene terephthalate copolymer. The polyether-ester copolymer protects the biologically active agent (including proteins, peptides, and small drug molecules) from degradation or denaturation and provides and essentially zero-order release.
ABSTRACT WORD COUNT: 70

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	9813	474
SPEC A	(English)	9813	17399
Total word count - document A			17873
Total word count - document B			0
Total word count - documents A + B			17873

6/3,AB/13 (Item 7 from file: 348)
DIALOG(R)File 348:European Patents

00889756
FUNCTIONAL FRAGMENT ANTIGEN OF TETANUS TOXIN AND TETANUS VACCINE
FUNKTIONELLES ANTIGENFRAGMENT VON TETANUSTOXIN UND TETANUSVAKZINE
ANTIGENE A FRAGMENT FONCTIONNEL DE LA TOXINE DU TETANOS, ET VACCIN CONTRE LE TETANOS
PATENT ASSIGNEE:
THE RESEARCH FOUNDATION FOR MICROBIAL DISEASES OF OSAKA UNIVERSITY, (1449700), Osaka University, 3-1, Yamadaoka, Suita-shi, Osaka 565, (JP) , (applicant designated states: BE;CH;DE;DK;FR;GB;IT;LI;NL)
INVENTOR:
MATSUDA, Morihiro, 37-4, Momoyamadai 3-chome, Suita-shi, Osaka 565, (JP)
LEGAL REPRESENTATIVE:
Blake, John Henry Francis (28371), Brookes & Martin High Holborn House 52/54 High Holborn, London WC1V 6SE, (GB)
PATENT (CC, No, Kind, Date): EP 845270 A1 980603 (Basic)
WO 9735612 971002
APPLICATION (CC, No, Date): EP 97907448 970324; WO 97JP976 970324
PRIORITY (CC, No, Date): JP 96106053 960323
DESIGNATED STATES: BE; CH; DE; DK; FR; GB; IT; LI; NL
INTERNATIONAL PATENT CLASS: A61K-039/08; C12N-015/00; C12N-015/31; C12P-021/02; C07K-014/33

ABSTRACT EP 845270 A1
A functional fragment antigen of tetanus toxin characterized in that the antigen comprises a fragment which is substantially the same as at least one type of the fragments obtained by cleaving at least one of the peptide bonds formed between the amino acid residues in the partial amino acid sequence present between the two cysteine residues participating in

the disulfide bridge present on the N-terminal side in the full-length amino acid sequence of a full-length tetanus toxin molecule, also cleaving the disulfide bridge itself, and further cleaving the non-covalent bonds between the amino acid residues that constitute the toxin molecule peptide, that it has a molecular weight of 90,000 to 110,000 as determined by SDS-polyacrylamide gel electrophoresis and an isoelectric point of 7.25(+-)0.5 as determined by isoelectric electrophoresis, and that it has an immunogenicity substantially equal to that of a full-length tetanus toxin molecule. This antigen keeps an immunogenicity as a tetanus vaccine antigen and is remarkably reduced in side effects. The invention also provides a process for the mass production of the functional fragment antigen, a vaccine containing this antigen, and a mixed vaccine comprising the above vaccine and a different vaccine.

ABSTRACT WORD COUNT: 194

LANGUAGE (Publication,Procedural,Application): English; English; Japanese
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	9823	442
SPEC A	(English)	9823	12613
Total word count - document A			13055
Total word count - document B			0
Total word count - documents A + B			13055

6/3,AB/14 (Item 8 from file: 348)
DIALOG(R)File 348:European Patents

00804385
Method for analyzing biological active substances
Verfahren zur Analyse von biologisch aktiven Substanzen
Methode pour l'analyse de substances avec l'activite biologiques
PATENT ASSIGNEE:
NISSHINBO INDUSTRIES, INC., (270162), 31-11, Nihonbashi Ningyocho, 2-chome, Chuo-ku, Tokyo 103, (JP), (applicant designated states: DE;FR;GB)
INVENTOR:
Suzuki, Osamu, Nisshinbo Ind. Inc., Tokyo Res. Ctr, 18-1 Nishi-arai, Sakae-cho 1-chome, Adachi-ku, Tokyo, (JP)
Sasaki, Naokazu, Nisshinbo Ind Inc, Tokyo Res. Ctr, 18-1 Nishi-arai, Sakae-cho 1-chome, Adachi-ku, Tokyo, (JP)
Ichihara, Tatsuo, Nisshinbo Ind Inc, Tokyo Res Ctr, 18-1 Nishi-arai, Sakae-cho 1-chome, Adachi-ku, Tokyo, (JP)
Okada, Sanae, Nisshinbo Ind. Inc., Tokyo Res. Ctr., 18-1 Nishi-arai, Sakae-cho 1-chome, Adachi-ku, Tokyo, (JP)
LEGAL REPRESENTATIVE:
Bannerman, David Gardner et al (28001), Withers & Rogers 4 Dyer's

Buildings Holborn, London, EC1N 2JT, (GB)
PATENT (CC, No, Kind, Date): EP 747703 A2 961211 (Basic)
EP 747703 A3 980909
APPLICATION (CC, No, Date): EP 96304158 960605;
PRIORITY (CC, No, Date): JP 95143715 950609
DESIGNATED STATES: DE; FR; GB
INTERNATIONAL PATENT CLASS: G01N-033/543; G01N-033/547; G01N-033/58; C12Q-001/68;

ABSTRACT EP 747703 A2
A method is provided, comprising the steps of reacting a biologically active first substance immobilized on a carrier with a second substance capable of specifically binding the first substance, and detecting a non-bound part of the second substance or a bound part of the second substance indirectly bound to the carrier through binding between the first and second substances so that the first substance or the second substance in a sample is analyzed, wherein the carrier carries a compound having 2 to 100 carbodiimide groups, and the first substance is immobilized on the carrier through the carbodiimide groups so that the active substance such as protein and nucleic acid is bound to the carrier conveniently, efficiently, and tightly.
ABSTRACT WORD COUNT: 138

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPAB96	342
SPEC A	(English)	EPAB96	10397
Total word count - document A			10739
Total word count - document B			0
Total word count - documents A + B			10739

6/3,AB/15 (Item 9 from file: 348)
DIALOG(R)File 348:European Patents

00793852
Variable fragments of immunoglobulins - use for therapeutic or veterinary purposes
Variable Fragmente von Immunglobulinen-Verwendung zur therapeutischen oder veterinaren Zwecken
Fragments variables d'immunoglobulines-utilisation therapeutique ou veterinaire
PATENT ASSIGNEE:
VRIJE UNIVERSITEIT BRUSSEL, (2116290), Pleinlaan 2, 1050 Brussel, (BE), (applicant designated states: GB)
INVENTOR:
Hamers, Raymond, Vijversweg 15, 1640 Sint-Genesius-Rode, (BE)

Muyldersmans, Serge, Inst. voor Molecul. Biologie, Vrije Universiteit Brussel, Paardenstraat 65, 1640 Sint-Genesius-Rode, (BE)
LEGAL REPRESENTATIVE:
Desaix, Anne et al (62911), Ernest Gutmann - Yves Plasseraud S.A. 3, rue Chauveau-Lagarde, 75008 Paris, (FR)
PATENT (CC, No, Kind, Date): EP 739981 A1 961030 (Basic)
APPLICATION (CC, No, Date): EP 95400932 950425;
PRIORITY (CC, No, Date): EP 95400932 950425
DESIGNATED STATES: GB
INTERNATIONAL PATENT CLASS: C12N-015/13; C07K-016/00; A61K-039/395;

ABSTRACT EP 739981 A1
The present invention relates to fragments, especially variable fragments of immunoglobulins which are by nature devoid of light chains these fragments being nevertheless capable of exhibiting a recognition and binding activity toward specific antigens.
The present invention further relates to the use of such immunoglobulin fragments formed of at least one heavy chain variable fragment or derived therefrom, for therapeutic or veterinary purposes and especially for passive immunotherapy or serotherapy.
ABSTRACT WORD COUNT: 84

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPAB96	2045
SPEC A	(English)	EPAB96	7092
Total word count - document A			9137
Total word count - document B			0
Total word count - documents A + B			9137

6/3,AB/16 (Item 10 from file: 348)
DIALOG(R)File 348:European Patents

00747981
ASSAY OF TETANUS- AND *BOTULINUM"** *TOXINS"**
BESTIMMUNG DER TETANUS- UND *BOTULINUM"** *TOXINE"**
DOSAGE DE TOXINES DU TETANOS ET DU BOTULISME
PATENT ASSIGNEE:
Microbiological Research Authority, (1820462), CAMR(Centre for Applied Microbiology & Research), Porton Down, Salisbury, Wiltshire SP4 0JG, (GB), (Proprietor designated states: all)
INVENTOR:
SHONE, Clifford, Charles, 44 Oakwood Grove, Alderbury, Salisbury SP5 3BN, (GB)
HALLIS, Bassam, 3 Avon Terrace, Salisbury, Wiltshire SP2 7BT, (GB)
JAMES, Benjamin, Arthur, Frederick, 22 Priory Close, Alderbury,

Salisbury, Wiltshire SP5 3TE, (GB)
QUINN, Conrad, Padraig, 36 St Francis Road, Salisbury, Wiltshire SP1 3QS, (GB)
LEGAL REPRESENTATIVE:
Schlich, George William et al (75591), Mathys & Squire 100 Gray's Inn Road, London WC1X 8AL, (GB)
PATENT (CC, No, Kind, Date): EP 763131 A1 970319 (Basic)
EP 763131 B1 990825
WO 9533850 951214
APPLICATION (CC, No, Date): EP 95921033 950602; WO 95GB1279 950602
PRIORITY (CC, No, Date): GB 9411138 940603
DESIGNATED STATES: AT; BE; CH; DE; DK; FR; GB; IT; LI; NL; SE
INTERNATIONAL PATENT CLASS: C12Q-001/37; C07K-016/40; G01N-033/68; G01N-033/543; G01N-033/569
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9934	685
CLAIMS B	(German)	9934	661
CLAIMS B	(French)	9934	778
SPEC B	(English)	9934	6065
Total word count - document A			0
Total word count - document B			8189
Total word count - documents A + B			8189

6/3,AB/17 (Item 11 from file: 348)
DIALOG(R)File 348:European Patents

00648931
ANTHRAX TOXIN FUSION PROTEINS AND USES THEREOF
ANTHRAX-TOXIN-FUSIONSPROTEINE UND DEREN VERWENDUNGEN
PROTEINES DE FUSION DE LA TOXINE DU BACILLE DU CHARBON ET LEURS UTILISATIONS
PATENT ASSIGNEE:
THE GOVERNMENT OF THE UNITED STATES OF AMERICA as represented by the SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES, (304190), National Institute of Health, Office of Technology Transfer, Westwood Building, Box OTT, Bethesda, MD 20892-9902, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
INVENTOR:
LEPPLA, Stephen H., 5612 Alta Vista Road, Bethesda, MD 20817, (US)
KLIMPEL, Kurt, 23816 Woodfield Road, Gaithersburg, MD 20882, (US)
ARORA, Naveen, G 110 Ashok Vihar, Phase I, Delhi 110052, (IN)
SINGH, Yogendra, SCIR Center for Biochemicals, University of Delhi, Mall Road, Delhi 110007, (IN)

LEGAL REPRESENTATIVE:
Thomson, Paul Anthony et al (36701), Potts, Kerr & Co. 15, Hamilton Square, Birkenhead Merseyside L41 6BR, (GB)
PATENT (CC, No, Kind, Date): EP 684997 A1 951206 (Basic)
EP 684997 B1 980819
WO 9418332 940818
APPLICATION (CC, No, Date): EP 94911385 940214; WO 94US1624 940214
PRIORITY (CC, No, Date): US 21601 930212; US 82849 930625
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: C12N-015/62; C12N-015/85; C12N-015/32; C07K-014/00; A61K-039/02; A61K-038/00;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9834	168
CLAIMS B	(German)	9834	134
CLAIMS B	(French)	9834	198
SPEC B	(English)	9834	21580
Total word count - document A			0
Total word count - document B			22080
Total word count - documents A + B			22080

6/3,AB/18 (Item 12 from file: 348)
DIALOG(R)File 348:European Patents

00601361
Pharmaceutical *compositions"** containing *botulinum"** *toxin"** and method of preparation.
Pharmazeutische Zusammensetzungen, die Botulinumtoxin enthalten und Verfahren zur Herstellung.
*Compositions"** pharmaceutiques contenant la toxine de botulinum et procede de preparation.
PATENT ASSIGNEE:
WISCONSIN ALUMNI RESEARCH FOUNDATION, (319666), P.O. Box 7365, Madison, WI 53705-7365, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
INVENTOR:
Schantz, Edward J., 5102 South Hill Drive, Madison WI 53705, (US)
Goodnough, Michael C., 6914 Harvest Hill Road, Madison WI 53717, (US)
Johnson, Eric A., 3901 Council Court, Madison WI 53711, (US)
LEGAL REPRESENTATIVE:
Ellis-Jones, Patrick George Armine (30442), J.A. KEMP & CO. 14 South Square Gray's Inn, London WC1R 5LX, (GB)
PATENT (CC, No, Kind, Date): EP 593176 A2 940420 (Basic)

EP 593176 A3 950301
APPLICATION (CC, No, Date): EP 93307656 930928;
PRIORITY (CC, No, Date): US 951604 920928
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61K-039/08;

ABSTRACT EP 593176 A2
A pharmaceutical *composition"** contains active lyophilized *botulinum"** *toxin"** type A, no sodium chloride and less than about 25 % inactive toxin is disclosed along with a method of preparing it.
ABSTRACT WORD COUNT: 32

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF2	190
SPEC A	(English)	EPABF2	1928
Total word count - document A			2118
Total word count - document B			0
Total word count - documents A + B			2118

6/3,AB/19 (Item 13 from file: 348)
DIALOG(R)File 348:European Patents

00509568
PROCESS FOR PREPARING A COOKED CURED MEAT PIGMENT.
VERFAHREN ZUR HERSTELLUNG EINES PULVERFORMIGEN PIGMENTES FUR GEKOCHTES POKELFLEISCH.
PROCEDE POUR LA PREPARATION D'UN PIGMENT EN POUDRE DE VIANDE CUITE ET SALEE.
PATENT ASSIGNEE:
SHAHIDI, Fereidoon, (1504050), 16 Russell Street,, St. John's, Newfoundland A1A 4E9, (CA), (applicant designated states: GB)
PEGG, Ronald B., (1504060), 57 Allandale Road, P.O. Box 325, Burton's Pond Apts., St. John's, Newfoundland A1B 3S7, (CA), (applicant designated states: GB)
INVENTOR:
SHAHIDI, Fereidoon, 16 Russell Street,, St. John's, Newfoundland A1A 4E9, (CA)
PEGG, Ronald B., 57 Allandale Road, P.O. Box 325, Burton's Pond Apts., St. John's, Newfoundland A1B 3S7, (CA)
LEGAL REPRESENTATIVE:
Loven, Keith James (47885), Loven & Co Claxlete House 62 Clasketgate, Lincoln LN2 1JZ, (GB)
PATENT (CC, No, Kind, Date): EP 554283 A1 930811 (Basic)
EP 554283 B1 950830
Searcher : Shears 308-4994

WO 9207476 920514
APPLICATION (CC, No, Date): EP 91917854 911024; WO 91CA377 911024
PRIORITY (CC, No, Date): US 602867 901024; US 743502 910809
DESIGNATED STATES: GB
INTERNATIONAL PATENT CLASS: A23L-001/275; A23B-004/20; A23B-004/24;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPAB95	508
CLAIMS B	(German)	EPAB95	534
CLAIMS B	(French)	EPAB95	652
SPEC B	(English)	EPAB95	13906
Total word count - document A			0
Total word count - document B			15600
Total word count - documents A + B			15600

6/3,AB/20 (Item 14 from file: 348)
DIALOG(R)File 348:European Patents

00506015
IMMUNOTOXIN *COMPLEX"**.
IMMUNTOXINKOMPLEX.
COMPLEXE IMMUNOTOXINIQUE.
PATENT ASSIGNEE:
TORAY INDUSTRIES, INC., (203533), 2-1, Nihonbashi Muromachi 2-chome Chuo-ku, Tokyo 103, (JP), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
YAMAZAKI, Shojiro, B-2,2-24, Tsunishi 2-chome, Kamakura-shi, Kanagawa 248, (JP)
SONE, Saburo, 1120-3, Yoshida-cho, Totsuka-ku, Yokohama-shi, Kanagawa 244, (JP)
KAJITA, Akemi, 936-16, Daigiri, Fujisawa-shi, Kanagawa 251, (JP)
LEGAL REPRESENTATIVE:
Kador & Partner (100211), Corneliusstrasse 15, W-8000 Munchen 5, (DE)
PATENT (CC, No, Kind, Date): EP 489931 A1 920617 (Basic)
EP 489931 A1 930224
WO 9200089 920109
APPLICATION (CC, No, Date): EP 91912070 910628; WO 91JP874 910628
PRIORITY (CC, No, Date): JP 90173516 900629
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-037/02; A61K-039/395; A61K-045/00;

ABSTRACT EP 489931 A1
An immunotoxin *complex"** prepared by combining an A-chain part of

toxin with an antibody which is readily combined with a tumor cell and incorporated therein. This *complex"** combines specifically with a tumor cell to efficaciously kill the cell, thus being useful for treating cancer. (see image in original document)
ABSTRACT WORD COUNT: 51

LANGUAGE (Publication,Procedural,Application): English; English; Japanese
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	174
SPEC A	(English)	EPABF1	3631
Total word count - document A			3805
Total word count - document B			0
Total word count - documents A + B			3805

6/3,AB/21 (Item 15 from file: 348)
DIALOG(R)File 348:European Patents

00448767
STABILIZED, POTENT GRF ANALOGS.
STABILISIERTE, STARKE GRF-ANALOGA.
ANALOGUES STABILISES DE GRF A ACTION PUISSANTE.
PATENT ASSIGNEE:
THE UPJOHN *COMPANY"**, (230490), 301 Henrietta Street, Kalamazoo, Michigan 49001, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;IT;LI;LU;NL;SE
INVENTOR:
KUBIAK, Teresa, M., 1523 Kickapoo Court, Kalamazoo, MI 49007, (US)
FRIEDMAN, Alan, R., 7646 Wendy Lane, Portage, MI 49002, (US)
LEGAL REPRESENTATIVE:
Perry, Robert Edward et al (41331), GILL JENNINGS & EVERY Broadgate House 7 Eldon Street, London EC2M 7LH, (GB)
PATENT (CC, No, Kind, Date): EP 477217 A1 920401 (Basic)
EP 477217 B1 941109
WO 9015821 901227
APPLICATION (CC, No, Date): EP 90908751 900530; WO 90US2923 900530
PRIORITY (CC, No, Date): US 368231 890616; US 427868 891027
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C07K-007/10; A61K-037/43;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	3001
CLAIMS B	(German)	EPBBF1	2893
CLAIMS B	(French)	EPBBF1	3401

SPEC B (English) EPBBF1 8123
Total word count - document A 0
Total word count - document B 17418
Total word count - documents A + B 17418

6/3,AB/22 (Item 16 from file: 348)
DIALOG(R)File 348:European Patents

00411795
PROCESS FOR PREPARING ASIALO GM1.
VERFAHREN ZUR HERSTELLUNG VON ASIALO GM1.
PROCEDE DE PREPARATION D'ASIALO GM1.
PATENT ASSIGNEE:
MARUKIN SHOYU CO., LTD., (930260), Ko 1850, Nouma, Uchinomi-cho, Shozu-gun, Kagawa 761-44, (JP), (applicant designated states: DE;IT)
INVENTOR:
SUGIMORI, Tsunetake, 2-180, Togariyama, Hirono-cho, Uji-shi, Kyoto 611, (JP)
TSUKADA, Yoji, Famiru-Fushimi B904, 23, Dewayashiki-cho, Fukakusa, Fushimi-ku, Kyoto-shi, Kyoto 612, (JP)
OHTA, Yasuhiro, 2-1, Sanbanwari, Gokanosho, Uji-shi, Kyoto 611, (JP)
LEGAL REPRESENTATIVE:
VOSSIUS & PARTNER (100311), Postfach 86 07 67, D-81634 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 451270 A1 911016 (Basic)
EP 451270 A1 930505
EP 451270 B1 950906
WO 9106662 910516
APPLICATION (CC, No, Date): EP 89911886 891030; WO 89JP1117 891030
PRIORITY (CC, No, Date): EP 89911886 891030; WO 89JP1117 891030
DESIGNATED STATES: DE; IT
INTERNATIONAL PATENT CLASS: C12P-019/26; C12N-009/24; C12N-009/24; C12R-001/06

ABSTRACT EP 451270 A1
The invention relates to a process for preparing asialo G(sub(Ml)) by the action of neuraminidase isozyme L on a ganglioside. The neuraminidase isozyme L used is one obtained from a culture medium of bacteria of the genus Arthrobacter and having the following physicochemical properties: function: capable of selectively producing asialo G(sub(Ml)) from gangliosides; molecular weight: about 88000 daltons (according to gel filtration chromatography and SDS-PAGE electrophoresis); optimum pH: 4.7 to 5.5 (in the case of using bovine cerebroganglioside as the substrate); and thermal stability: up to 60 (degree)C.
ABSTRACT WORD COUNT: 92

LANGUAGE (Publication,Procedural,Application): English; English; Japanese
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPAB95	327
CLAIMS B	(German)	EPAB95	279
CLAIMS B	(French)	EPAB95	341
SPEC B	(English)	EPAB95	2089
Total word count - document A			0
Total word count - document B			3036
Total word count - documents A + B			3036

6/3,AB/23 (Item 17 from file: 348)
DIALOG(R)File 348:European Patents

00411781
PROCESS FOR PREPARING GANGLIOSIDE GM1.
VERFAHREN ZUR HERSTELLUNG VON GANGLIOSID GM1.
PROCEDE DE PREPARATION DE GANGLIOSIDE GM1.
PATENT ASSIGNEE:
MARUKIN SHOYU CO., LTD., (930260), Ko 1850, Nouma, Uchinomi-cho, Shozu-gun, Kagawa 761-44, (JP), (applicant designated states: DE;IT)
INVENTOR:
SUGIMORI, Tsunetake, 2-180, Togariyama Hirono-cho, Uji-shi Kyoto 611, (JP)
TSUKADA, Yoji, Famiru-Fushimi B904 23, Dewayashiki-cho Fukakusa, Fushimi-ku, Kyoto-shi Kyoto 612, (JP)
OHTA, Yasuhiro, 2-1, Sanbanwari Gokanosho, Uji-shi Kyoto 611, (JP)
LEGAL REPRESENTATIVE:
VOSSIUS & PARTNER (100311), Postfach 86 07 67, D-81634 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 451267 A1 911016 (Basic)
EP 451267 A1 930428
EP 451267 B1 950809
WO 9106663 910516
APPLICATION (CC, No, Date): EP 89911863 891030; WO 89JP1118 891030
PRIORITY (CC, No, Date): EP 89911863 891030; WO 89JP1118 891030
DESIGNATED STATES: DE; IT
INTERNATIONAL PATENT CLASS: C12P-019/26; C12N-009/24; C12N-009/24; C12R-001/06

ABSTRACT EP 451267 A1
The invention relates to a process for preparing ganglioside G(sub(Ml)) by the action of neuraminidase isozyme S on a ganglioside. The neuraminidase isozyme S used is one obtained from a culture medium of bacterial of the genus Arthrobacter and having the following physicochemical properties; function: capable of selectively producing ganglioside G(sub(Ml)) from gangliosides; molecular weight: about 52000 daltons (according to gel filtration chromatography and SDS-PAGE electrophoresis); optimum pH: 3.8 to 4.4 (in the case of using bovine cerebroganglioside as the substrate); and thermal stability: up to 60

(degree)C.
ABSTRACT WORD COUNT: 92

LANGUAGE (Publication,Procedural,Application): English; English; Japanese
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPAB95	326
CLAIMS B	(German)	EPAB95	281
CLAIMS B	(French)	EPAB95	343
SPEC B	(English)	EPAB95	2093
Total word count - document A			0
Total word count - document B			3043
Total word count - documents A + B			3043

6/3,AB/24 (Item 18 from file: 348)
DIALOG(R)File 348:European Patents

00384189
MACROCYCLIC COMPLEXES OF YTTRIUM, THE LANTHANIDES AND THE ACTINIDES HAVING PERIPHERAL COUPLING FUNCTIONALITIES
MAKROCYCLISCHE KOMPLEXE VON YTTRIUM, DEN LANTHANIDEN UND DEN ACTINIDEN MIT PERIPHEREN KUPPLUNGSFUNKTIONALITATEN
COMPOSES MACROCYCLIQUES D'YTTRIUM, DE LANTHANIDES ET D'ACTINIDES A FONCTIONS PERIPHERIQUES DE LIAISON
PATENT ASSIGNEE:
Vallarino, Lidia M., (1871350), 1009 West Avenue, Richmond, VA 23220, (US), (applicant designated states: CH;DE;FR;GB;IT;LI;SE)
Leif, Robert C., (1871360), 5648 Toyon Road, San Diego, CA 92115, (US), (applicant designated states: CH;DE;FR;GB;IT;LI;SE)
INVENTOR:
Vallarino, Lidia M., 1009 West Avenue, Richmond, VA 23220, (US)
Leif, Robert C., 5648 Toyon Road, San Diego, CA 92115, (US)
LEGAL REPRESENTATIVE:
Nettleton, John Victor et al (34281), Abel & Imray 20 Red Lion Street, London WC1R 4PQ, (GB)
PATENT (CC, No, Kind, Date): EP 369000 A1 900523 (Basic)
EP 369000 A1 930602
EP 369000 B1 990421
WO 8911868 891214
APPLICATION (CC, No, Date): EP 89907468 890530; WO 89US2347 890530
PRIORITY (CC, No, Date): US 200220 880531; US 353823 890522
DESIGNATED STATES: CH; DE; FR; GB; IT; LI; SE
INTERNATIONAL PATENT CLASS: A61K-051/00; A61K-049/00; C07F-009/80; C07D-327/00; C07D-311/00; C07D-471/18; G01N-033/533;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English

FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9916	1306
CLAIMS B	(German)	9916	1300
CLAIMS B	(French)	9916	1524
SPEC B	(English)	9916	12089
Total word count - document A			0
Total word count - document B			16219
Total word count - documents A + B			16219

6/3,AB/25 (Item 19 from file: 348)
DIALOG(R)File 348:European Patents

00307444
Protein 7B2, recombinant DNA, cDNA and mRNA, antibodies for 7B2, and a method of detecting 7B2.
Protein 7B2, rekombinante DNA, cDNA und mRNA Antikorper fur 7B2 und Verfahren zum Nachweis von 7B2.
Proteine 7B2, ADN recombinant, ADN complementaire et ARN messager, anticorps contre 7B2 et methode de detection de 7B2.
PATENT ASSIGNEE:
Stichting Katholieke Universiteit, (572550), Toernooiveld 1, NL-6525 ED Nijmegen, (NL), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Martens, Gerardus Julianus Maria, Sleedoornstraat 11, NL-6523 GE Nijmegen, (NL)
LEGAL REPRESENTATIVE:
Smulders, Theodorus A.H.J., Ir. et al (21191), Vereenigde Octrooibureaux Nieuwe Parklaan 107, NL-2587 BP 's-Gravenhage, (NL)
PATENT (CC, No, Kind, Date): EP 315254 A1 890510 (Basic)
APPLICATION (CC, No, Date): EP 88202395 881028;
PRIORITY (CC, No, Date): NL 872590 871030
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C12N-015/00; C12P-021/02; C12P-021/00; G01N-033/577;

ABSTRACT EP 315254 A1
The invention provides recombinant DNA comprising genetic information for 7B2 protein, and a process for preparing protein 7B2 by expression of such recombinant DNA. The invention also provides antibodies with a specificity for protein 7B2 and a method of detecting 7B2 protein or mRNA, wherein such antibodies or labelled RNA or DNA probes of 7B2 are used.
ABSTRACT WORD COUNT: 61

LANGUAGE (Publication,Procedural,Application): English; English; English

FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	179
SPEC A	(English)	EPABF1	5593
Total word count - document A			5772
Total word count - document B			0
Total word count - documents A + B			5772

6/3,AB/26 (Item 20 from file: 348)
DIALOG(R)File 348:European Patents

00245162
Botulinus toxin neutralizer.
Neutralisierung von Botulinus-Toxin.
Neutralisant de la toxine Botulinus.
PATENT ASSIGNEE:
KABUSHIKI KAISHA YAKULT HONSHA, (316160), 1-19, Higashishinbashi 1-chome, Minato-ku Tokyo 105, (JP), (applicant designated states: CH;DE;FR;GB;LI;NL;SE)
INVENTOR:
Nagai, Yoshitaka, No. 1-29-18, Akazutumi, Setagaya-ku Tokyo, (JP)
Takamizawa, Koutaro, No. 5-3-10-203, Higashicho, Irima Saitama, (JP)
Tanaka, Ryuichiro, No. 2-38-8, Wakabacho, Tachikawa Tokyo, (JP)
Takayama, Hiroo, No. 4-35-17-402, Midoricho, Tokorozawa Saitama, (JP)
Sakurai, Toshizo, No. 2-7-19, Nakahara Mitaka, Tokyo, (JP)
Mutai, Masahiko, No. 4-988, Shimizu Higashiyamato, Tokyo, (JP)
LEGAL REPRESENTATIVE:
Brewer, Leonard Stuart et al (42871), SANDERSON & CO. European Patent Attorneys 34, East Stockwell Street, Colchester Essex CO1 1ST, (GB)
PATENT (CC, No, Kind, Date): EP 235957 A2 870909 (Basic)
EP 235957 A3 900117
EP 235957 B1 930407
APPLICATION (CC, No, Date): EP 87300962 870203;
PRIORITY (CC, No, Date): JP 8620066 860203
DESIGNATED STATES: CH; DE; FR; GB; LI; NL; SE
INTERNATIONAL PATENT CLASS: A61K-031/20;

ABSTRACT EP 235957 A2
A botulinus toxin neutralizer comprises at least one fatty acid having at least 12 carbon atoms. Such a fatty acid may be a saturated fatty acid such as lauric acid, myristic acid, palmitic acid, stearic acid, nonadecanoic acid, arachidic acid or behenic acid, or an unsaturated fatty acid such as oleic acid. The toxin neutralizer acts as if it were an antagonistic receptor for botulinus toxin and, when encountering botulinus toxin in the human body, it combines directly with the toxin and prevents the toxin from combining with the neuromuscular tissues of the human body. Hence the neutralizer prevents the outbreak of botulism.

The toxin thus neutralized and affixed to the botulinus toxin is excreted from the human body. The botulinus toxin neutralizer can be manufactured easily and economically from a naturally occurring glyceride and is thus far less costly than the known antitoxin of ganglioside GT1b produced from bovine brain.

ABSTRACT WORD COUNT: 155

LANGUAGE (Publication,Procedural,Application): English; English; English

FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	355
CLAIMS B	(German)	EPBBF1	231
CLAIMS B	(French)	EPBBF1	306
SPEC B	(English)	EPBBF1	2615
Total word count - document A			0
Total word count - document B			3507
Total word count - documents A + B			3507

6/3,AB/27 (Item 1 from file: 357)

DIALOG(R)File 357:Derwent Biotechnology Abs

0037703 DBA Accession No.: 85-08492

Production of monoclonal antibodies against Clostridium botulinum type E derivative toxin - hybridoma generation and monoclonal antibody production

AUTHOR: Kamata Y; Kozaki S; Nagai T; Sakaguchi G

CORPORATE SOURCE: Department of Veterinary Science, College of Agriculture, University of Osaka Prefecture, Sakai-shi, Osaka 591, Japan.

JOURNAL: FEMS Microbiol.Lett. (26, 3, 305-09) 1985

CODEN: FMLED7

LANGUAGE: English

ABSTRACT: Clostridium botulinum type E derivative toxin was prepared by established methods. The derivative toxin was purified by DEAE-Sephadex chromatography and toxoided by dialysis against 0.4% formalin in 0.1 M *phosphate"** *buffer"** , pH 7.0. BALB/c mice were immunized by injecting 2 doses of the toxoid emulsified with Freund's complete adjuvant and an additional dose without adjuvant. Spleen cells from the immunized mice were fused with cells from the P3X63-Ag8-U1 mouse myeloma line using PEG. Hybridomas produced were selected in HAT culture medium and those secreting monoclonal antibodies were cloned by limiting dilution. For mass production of the monoclonal antibodies, the cloned hybridomas were injected i.p. into Pristane-primed BALB/c mice for the production of ascites fluid. 5 Monoclonal antibodies were obtained. 3 Of them possessed neutralizing activity comparable to that of polyclonal antibody. The monoclonal antibodies bound to different sites on the type E toxin molecule. Using these monoclonal antibodies, it may be possible to separate fragments of type E toxin by affinity chromatography and to scrutinize the structure-function relationship of

*botulinum"** *toxins"**. (17 ref)
? ds; t 11/3,ab/1

-Author(s)

Set	Items	Description
S7	168	AU=(MOYER, E? OR MOYER E?)
S8	12	AU=(HIRTZER, P? OR HIRTZER P?)
S9	1	S7 AND S8
S10	1	(S7 OR S8) AND S1
S11	1	(S9 OR S10) NOT S5

>>>No matching display code(s) found in file(s): 65, 113

11/3,AB/1 (Item 1 from file: 348)
DIALOG(R)File 348:European Patents

01149591
STABLE LIQUID FORMULATIONS OF *BOTULINUM"** *TOXIN"**
STABILISIERTE FLUSSIGE ARZNEIZUBEREITUNGEN ENTHALTEND *BOTULINUM"** *TOXIN"**
FORMULATIONS LIQUIDES STABLES DE LA TOXINE DE BOTULINUM
PATENT ASSIGNEE:
Elan Pharmaceuticals, Inc., (2709860), 800 Gateway Boulevard, South San Francisco, CA 94080, (US), (Applicant designated States: all)
INVENTOR:
*MOYER, Elizabeth"**, 435 Marin Avenue, Mill Valley, CA 94941, (US)
*HIRTZER, Pamela"**, 291 Scenic Avenue, Piedmont, CA 94611, (US
PATENT (CC, No, Kind, Date):
WO 0015245 000323
APPLICATION (CC, No, Date): WO 99945649 990909; WO 99US20912 990909
PRIORITY (CC, No, Date): US 99870 P 980911
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61K-038/16; A61K-047/02; A61K-047/12
LANGUAGE (Publication,Procedural,Application): English; English; English
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26sep00 14:16:16 User219783 Session D1643.2